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13. Abstract (Maximum 200 Words) (abstract should contain no proprietary or confidential information) To determine whether failure to perform axillary dissection or irradiation is associated with decreased survival in women with early-stage breast cancer, we studied 26,290 women aged ≥25 in 1988-93 from the Surveillance, Epidemiology and End Results (SEER) data and 5,328 women aged ≥65 in 1991-93 from SEER-Medicare data, who received BCS. About 27% of women aged ≥25 receiving BCS did not receive axillary dissection, most of whom (74%) were age ≥65. Women receiving BCS with axillary dissection had lower 7-year breast cancer-specific mortality than did those without dissection (hazard ratio=0.53, 95% confidence interval: 0.44-0.63). We found a relationship between receipt of axillary dissection and radiotherapy on survival of older women. Women who received either axillary dissection or radiotherapy experienced similar survivals to those who received both, while women who received neither treatment experienced poorer survival (hazard ratio=1.76, 1.23-2.52), after controlling for demographics, tumor size and comorbidity. In conclusion, women who receive neither axillary dissection nor radiotherapy experience an increased risk of death from breast cancer. The lack of improvement in past two decades in survival of older women with breast cancer may be explained in part by the increasing use of treatments that do not address potential tumor in axillary nodes.				
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Introduction

Over the past several decades, the treatment patterns of breast cancer have changed dramatically, including the adoption of breast-conserving surgery (BCS) and the greater use of combination chemotherapy and hormone therapy for early-stage breast cancer (local or regional stage).¹⁻⁶ It has been well documented that the recurrence and survival after BCS plus radiation was equivalent to that of modified radical mastectomy, while preserving the breast and maximizing the quality of life.¹⁻⁶ For these reasons, the increasing numbers of older women with breast cancer are receiving BCS.⁷⁻⁹ Axillary node dissection is a component of modified radical mastectomy, and also is commonly used in BCS.^{5,10,11} However, substantial numbers of them are not receiving either axillary dissection or adjuvant radiation or chemotherapy.^{7,12-16} Although the sentinel lymph node dissection may have potential to replace for axillary dissection, to date it has still not been considered for routine use.¹⁷ The previous reports on the percentages receiving axillary dissection by stage may be misleading,^{7,18} because the major means of distinguishing regional from local stage is by axillary dissection. Thus, there is a misclassification bias of underreporting regional stage tumor in women without axillary dissection. Our aim was to determine whether failure to perform axillary dissection is associated with decreased survival in women with early-stage breast cancer. We studied 26,290 women with early-stage breast cancer aged ≥ 25 in 1983-1993 who received BCS, using data from the Surveillance, Epidemiology and End Results Program and Medicare.

Body

This section described the research accomplishments associated with each task outlined in the Statement of Work in the original proposal on page 12.

Statement 1. To identify the study population from the SEER-Medicare data base and to construct an analytic file with study variables:

We identified several cohorts of women with breast cancer diagnosed in 1991 through 1996 from the SEER-Medicare linked data (see Appendix 1 to 9 for copies of articles published or in press). For example, in a study of the impact of axillary dissection on survival of women with breast cancer, we identified 5,328 women aged 65 or older with breast cancer in the analytic files (see copy of the article in Appendix 9).

Statement 2. To generate descriptive tables and identify any outliers or inconsistencies in the data file:

See Appendices 1 to 9 for copies of articles published or in press.

Statement 3. To test assumptions of the proportional hazards model for survival and late cancer directed therapy:

See Appendix 9 for the survival analysis, and Appendices 2 to 4 for cancer directed therapies.

Statement 4. To conduct analyses of axillary treatment and survival:

See Appendix 9 for the analyses of axillary treatment and survival.

Statement 5. To conduct analyses of late cancer-related surgery, late radiotherapy and late chemotherapy:

See Appendices 1 to 4 and 9 for the analyses of these therapies.

Statement 6. Write reports and prepare papers for publications.

See Appendices 1 to 9 for articles published or in press, and also see the "Reportable Outcomes" section below.

Key Research Accomplishments

The findings of this study can be summarized as follows.

First, substantial numbers of older women receiving breast-conserving surgery do not receive axillary dissection.⁷

Second, of those women not receiving axillary dissection, most also do not receive either adjuvant radiation therapy or chemotherapy.^{7,8,12-16} In other words, they receive no therapy directed at occult cancer in the axillary nodes. The percentage of older women who receive no therapy to their axillary nodes has been steadily increasing over the past decade.^{7-9,12}

Third, patients receiving breast-conserving surgery without axillary dissection experience significantly worse survivals than those who do, after controlling for other factors known to affect survival.

Finally, there is an interaction between receipt of axillary dissection and radiation therapy on survival, such that women who receive either axillary dissection or radiation therapy experience similar survivals to those who receive both axillary dissection and radiation, while women who receive neither treatment experience substantially poorer survivals.

Reportable outcomes

Articles published or in press in peer-reviewed journals:

1. Du XL, Freeman DH, Syblik DA. What drove changes in the use of breast conserving surgery for breast cancer since the early 1980s? The role of the clinical trial, celebrity action and an NIH consensus statement. *Breast Cancer Research and Treatment*. 62(1):71-79; 2000.
2. Du XL, Freeman JL, Warren JL, Nattinger AB, Zhang D, Goodwin JS. Accuracy and completeness of Medicare claims data for surgical treatment of breast cancer. *Medical Care*. 38(7):719-727; 2000.
3. Du XL, Goodwin JS. Patterns of use of chemotherapy for breast cancer in older women: Findings from Medicare claims data. *Journal of Clinical Oncology*. 2001;19(5):1455-1461.
4. Du XL, Goodwin JS. Increase of Chemotherapy Use in Older Women with Breast Cancer from 1991 to 1996. *Cancer* (in press).

Abstracts published in academic journals:

1. Du XL, Freeman JL, Nattinger AB, Goodwin JS. The effect of axillary node dissection on survival in women with early stage breast cancer. *American Journal of Epidemiology*. 2000;151(suppl):S64.
2. Du XL, Goodwin JS. Patterns of use of chemotherapy for breast cancer in older women: findings from Medicare claims data. *Gerontologist*. 2000;40(Special Issue I):344-345.
3. Du XL, Goodwin JS. Increase of Chemotherapy Use in Older Women with Breast Cancer from 1991 to 1996. *American Journal of Epidemiology*. 2001;153(suppl):S108.
4. Du XL, Goodwin JS. Using Medicare Data to Examine the Patterns of Chemotherapy Use for Older Women with Breast Cancer. *American Journal of Epidemiology*. 2001;153(suppl):S226.

Presentations at the scientific meetings:

1. Du XL, Freeman JL, Warren JL, Nattinger AB, Zhang D, Goodwin JS. Accuracy and completeness of Medicare claims data for surgical treatment of breast cancer. Presented at the scientific meeting of the Academy for Health Services Research and Health Policy, Los Angeles, CA, June 25-27, 2000.
2. Du XL, Freeman DH, Syblik DA. What drove changes in the use of breast conserving surgery for breast cancer since the early 1980s? The role of the clinical trial, celebrity action and an NIH consensus statement. Presented at the scientific meeting of the Academy for Health Services Research and Health Policy, Los Angeles, CA, June 25-27, 2000.

3. Du XL, Freeman JL, Nattinger AB, Goodwin JS. The effect of axillary node dissection on survival in women with early stage breast cancer. Presented at the Forum on Aging, UTMB, TX, September 27, 2000.
4. Du XL, Goodwin JS. Patterns of use of chemotherapy for breast cancer in older women: findings from Medicare claims data. Presented at the Forum on Aging, UTMB, TX, September 27, 2000.
5. Du XL, Goodwin JS. Patterns of use of chemotherapy for breast cancer in older women: Findings from Medicare claims data. Presented at the Gerontologic Society of America Annual Meeting, Washington, DC, November 20-22, 2000.
6. Du XL, Goodwin JS. Increase of Chemotherapy Use in Older Women with Breast Cancer from 1991 to 1996. Presented at the Congress of Epidemiology, a Joint Meeting of the American College of Epidemiology, American Public Health Association Epidemiology Section, Canadian Society for Epidemiology and Biostatistics, and Society for Epidemiologic Research, Toronto, Canada, June 13-16, 2001.
7. Du XL, Goodwin JS. Using Medicare Data to Examine the Patterns of Chemotherapy Use for Older Women with Breast Cancer. Presented at the Congress of Epidemiology, a Joint Meeting of the American College of Epidemiology, American Public Health Association Epidemiology Section, Canadian Society for Epidemiology and Biostatistics, and Society for Epidemiologic Research, Toronto, Canada, June 13-16, 2001.

Manuscripts submitted for publications

Du XL, Freeman JL, Nattinger AB, Goodwin JS. Survival of Women After Breast Conserving Surgery for Early Stage Breast Cancer. Submitted.

Conclusions

In conclusion, the combination of no axillary dissection plus no radiation after BCS is associated with an unacceptably high level of deaths from breast cancer. The lack of improvement in the past two decades in survival of older women with breast cancer may be explained in part by the increasing use of treatments that do not address potential tumor in axillary nodes. Further research will be performed to look at hormone therapy and social economic factors in relation to the effect of axillary node dissection on clinical outcomes.

From the performance of this study, a great deal has been learnt about using the large databases such as Medicare claims for research. Considerable experience has been gained in using Medicare data to explore comorbidity status and treatment procedures, and in performing survival analyses.

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18. Bland KI, Scott-Conner CE, Menck H, Winchester DP. Axillary dissection in breast-conserving surgery for stage I and II breast cancer: a National Cancer Data Base study of patterns of omission and implications for survival. *J Am Coll Surg* 1999;188:586-95.

Appendix

There are a total of 9 appendices attached.

Appendix 1 to 4. Reprints of the 3 articles published and the hard copy of an article in press.

1. Du XL, Freeman DH, Syblik DA. What drove changes in the use of breast conserving surgery for breast cancer since the early 1980s? The role of the clinical trial, celebrity action and an NIH consensus statement. *Breast Cancer Research and Treatment*. 62(1):71-79; 2000.
2. Du XL, Freeman JL, Warren JL, Nattinger AB, Zhang D, Goodwin JS. Accuracy and completeness of Medicare claims data for surgical treatment of breast cancer. *Medical Care*. 38(7):719-727; 2000.
3. Du XL, Goodwin JS. Patterns of use of chemotherapy for breast cancer in older women: Findings from Medicare claims data. *Journal of Clinical Oncology*. 2001;19(5):1455-1461.
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Report

What drove changes in the use of breast conserving surgery since the early 1980s? The role of the clinical trial, celebrity action and an NIH consensus statement

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Key words: breast cancer, breast conserving surgery, clinical trial, celebrity, consensus statement

Summary

Background. Three important events in the history of breast cancer treatment occurred between 1983 and 1995: a large clinical trial, first lady Nancy Reagan's choice of mastectomy and the publishing of an NIH consensus statement.

Objective. To assess the effects of these events on use of breast conserving surgery (BCS).

Research design. Data from the cohort study of the surveillance, epidemiology and end results (SEER) Program from 1983 to 1995 were divided into four periods: Baseline, Trial, Celebrity, and Consensus.

Subjects. Of the women, 169,466 diagnosed with early stage breast cancer in nine SEER areas.

Measures. Monthly percentages of BCS.

Results. A linear regression model generated a separate intercept and slope term for four time periods, adjusting for demographic characteristics of breast cancer patients. For the Baseline, Celebrity and Consensus Periods, slopes indicated an increasing use of BCS which varied between 0.24% and 0.28% per month. Slopes for these three periods were not statistically different ($p = 0.120$). In contrast, there was no change in use of BCS during the trial period ($p = 0.247$). We tested the magnitude of discontinuity between periods. At the beginning of the trial, celebrity and consensus periods, there were increases in BCS of 5.54% ($p < 0.001$), -3.55% ($p < 0.001$), and 2.37% ($p < 0.001$), respectively.

Conclusions. The use of BCS was substantially affected by the reports of a clinical trial of BCS and by celebrity action. These effects were abrupt but transient. The NIH consensus statement stimulated a small change in use of BCS and may be an important intervention for maintaining the increasing trend in use of BCS since the 1990s.

Introduction

For many decades, mastectomy has been a major and dominant surgical treatment for breast cancer. Since the early 1980s, a series of clinical trials demonstrated the efficacy of breast conserving surgery (BCS) as compared to mastectomy [1–3]. In March 1985, publication of the 5-year results of a large US randomized prospective clinical trial, the National Surgical Adjuvant Breast Project B-06 trial, received wide public and professional media attention [3–5]. The trial randomized 1,855 women with stage I or stage

II breast cancer. Following this report, publications from many other clinical trials and population-based observational studies supported the scientific justification for the BCS trial [6–19]. This eventually led the National Institutes of Health (NIH) to convene a Consensus Development Conference on 18–21 June 1990 on the treatment of early stage breast cancer [20]. The consensus statement was developed and published in *JAMA* in January 1991, an official journal of the American Medical Association with wide circulation and high visibility [20]. However, there was no study conducted to show how the clinical trials affected the

trend toward receipt of BCS in women with breast cancer. A number of studies addressed the effect of the previous NIH consensus conferences on treatment for breast cancer [21, 22], prostate cancer [23], and other disorders [24, 25]. They concluded that conference recommendations had little effect on physicians' behavior. A study done in Seattle assessed the impact of the most recent 1991 consensus conference on the use of BCS for breast cancer [26]. It showed that the percentage of BCS seemed to increase gradually since 1988 without obvious fluctuations. Therefore, it may not be appropriate to simply compare the percentage of BCS after the conference with that before the conference, and then attribute the increase to the effect of the consensus conference. The more appropriate way to address the effect of such an event on the use of BCS would be to estimate a simple linear regression between time and percentage of BCS for different time periods (before and after conference). Then the slopes and intercepts of such regressions could be compared across the time periods. The process of diffusion of the treatment is further complicated by the decision of the former US President Ronald Reagan's wife, Nancy Reagan, to undergo a modified radical mastectomy after she was diagnosed for an early stage breast cancer [27, 28]. This event has been shown to be significant in affecting the choice of surgery by the US women with breast cancer [29]. Our present study attempted to examine the effects of these three important events on the whole trend in the use of BCS from the early 1980s to the mid 1990s, in order to determine whether the large clinical trial, celebrity action, and the publication of the NIH consensus statement all have an immediate impact on the use of BCS.

Methods

Data base

This study uses data from the surveillance, epidemiology and end results (SEER) 1973–95 Public use data set (CD-ROM released in April 1998). The SEER program supports population-based prospective tumor registries in four metropolitan areas (San Francisco/Oakland, Detroit, Atlanta, Seattle) and five states (Connecticut, Iowa, New Mexico, Utah and Hawaii), covering approximately 10% of the US population [30]. The registries attempt to identify all newly diagnosed (incident) breast cancer cases since 1973 from multiple reporting sources such as hospitals, outpatient clinics, laboratories, private medical

practitioners, nursing/convalescent homes/hospices, autopsy reports and death certificates [31]. Recorded data include tumor location and size; lymph node and distant organ metastases; histologic type and grade of tumor; demographic characteristics such as age, gender, race and marital status; and type of treatments provided in the first four months of therapy after diagnosis. The SEER public use data set includes types of surgical procedures and radiation therapy.

Study population

The eligible subjects for this study included 171,795 female patients with local or regional stage breast cancer diagnosed between 1983 and 1995, because the detailed surgical treatment was available in SEER only since January 1983. Of these, 2,329 were excluded from the analysis because the information was missing about cancer directed surgery (2,262) or the month of diagnosis (67), leaving 169,466 patients for the final analysis.

Measures of surgery for breast cancer

Cancer-directed surgery was defined as either mastectomy, which includes total/subcutaneous/radical/modified radical mastectomy, or BCS, which includes segmental mastectomy, lumpectomy, quadrantectomy, tylectomy, wedge resection, nipple resection, excisional biopsy, or partial mastectomy unspecified.

Early stage breast cancer refers to both local and regional stage breast cancer. The SEER system defines local stage as an invasive neoplasm confined entirely to the organ of origin. Regional stage is defined as a neoplasm that has extended (1) beyond the limits of the organ or origin directly into surrounding organs or tissues; or (2) into regional lymph nodes by way of the lymphatic system; or (3) by a combination of extension and regional lymph nodes. SEER uses the best available clinical and surgical information for staging tumors.

Analysis

We believe the months from January 1983 through December 1995 can be divided into four distinct periods based on the date of three important events. The baseline period is from January 1983 through February 1985. The baseline period ends when the first large scale US clinical trial of BCS was published on March 14, 1985. The second period, 'the trial period' begins from March 1985 and continues through September

Table 1. Characteristics (in percentage) of patients diagnosed with breast cancer in different time periods of events between 1983 and 1995

	Baseline period	Trial period	Celebrity period	Consensus period	Total
Age (years)					
<45	14.9	14.3	14.2	13.7	14.1
45-54	17.2	16.5	17.1	19.7	18.1
55-64	24.6	23.7	21.5	20.0	21.7
65-74	24.1	25.3	25.7	25.0	25.1
75 +	19.2	20.1	21.5	21.6	21.0
Race					
White	89.3	88.5	88.1	86.4	87.6
Black	6.7	6.7	6.9	7.4	7.1
Other	3.8	4.4	4.7	5.5	4.9
Unknown	0.2	0.4	0.3	0.7	0.5
Marital status					
Married	56.6	56.3	56.6	55.8	56.2
Unmarried	40.9	41.2	41.0	41.8	41.4
Unknown	2.6	2.5	2.4	2.4	2.4
Tumor stage					
Local stage	58.0	62.2	66.5	69.9	66.0
Regional stage	42.0	37.8	33.5	30.1	34.0
Total	22,223 (100.0)	31,669 (100.0)	43,379 (100.0)	72,195 (100.0)	169,466 (100.0)

1987, just before Nancy Reagan had a modified radical mastectomy on October 17, 1987. The third period, 'the celebrity period', runs from October 1987 through December 1990. This third period ends just prior to the publication of the NIH consensus development conference on January 16, 1991. The final period runs from January 1991 through December 1995, which is the last date for which we had data. For simplicity we will refer to the periods as:

- (1) Baseline: January 1, 1983–February 28, 1985;
- (2) Trial: March 1, 1985–September 30, 1987;
- (3) Celebrity: October 1, 1987–December 31, 1990; and
- (4) Consensus: January 1, 1991–December 31, 1995.

Previous investigators have used logistic regression to analyze these data, but as noted by many statisticians, including Cox and Wermuth [32], '... linear regressions ... [where] the range of fitted values is not extreme (e.g., between 0.2 and 0.8), are virtually indistinguishable from logistic and probit regressions'. For

ease of interpretation, we fit a simple linear regression model to the percentage of breast cancer patients who received BCS. This model is constructed as separate straight line models of the percentage of women receiving BCS within each period. This percentage can be represented as:

$Y_{ij} = 100$ if woman j with localized breast cancer in period i had BCS; and, 0 otherwise; where $i = 1, 2, 3$ or 4, $j = 1, \dots, n_i$, and n_i is the number of women receiving treatment in period i .

The combined regression model has the following form:

$$Y_{ij} = \alpha_i + \beta_i T_{ij} + \sum_{h=1}^H \gamma_h X_{hij} + \varepsilon_{ij},$$

where h indexes covariates and $h = 1, \dots, H$.

Here α_i and β_i are the separate intercepts and slopes for each period i , $i = 1, 2, 3, 4$ and γ_h are the coefficients of the covariates. The month is represented by T_{ij} and runs from 1 to 156. Subject characteristics (age, race, marital status, cancer stage and SEER area) are represented by the X_{hij} . The statistical tests re-

Table 2. Percentage of women with early stage breast cancer who received breast conserving surgery (BCS) in each time period between 1983 and 1995 by patient and tumor characteristics

	Baseline period	Trial period	Celebrity period	Consensus period
Total% of BCS	17.6	26.3	27.5	42.6
Age (years)				
<45	22.5	31.5	31.1	42.7
45–54	17.4	28.0	29.8	46.2
55–64	15.4	25.0	27.6	44.2
65–74	14.5	22.9	24.3	41.0
75+	20.8	27.3	27.2	39.7
Race				
White	17.7	26.7	27.8	42.9
Black	17.7	25.4	27.6	41.8
Other	15.9	20.3	22.9	38.9
Unknown	17.0	39.3	41.0	49.9
Marital status				
Married	16.7	25.9	27.6	43.1
Unmarried	18.6	26.6	27.4	41.5
Unknown	23.2	32.7	29.5	50.2
Tumor stage				
Local stage	21.7	32.1	33.0	49.3
Regional stage	11.9	16.8	16.6	27.1

All percentages are the number of women with early stage breast cancer who received BCS in the specific variable category (e.g. age 45–54) during the specified time period.

quire that the error terms ε_{ij} be approximately normal with mean zero and fixed variance. It is important to recognize that the estimators will be unbiased even if the errors are not normally distributed as long as the model is approximately linear. We used the monthly rate of BCS as the unit of analysis because it is more sensitive to detect the changes by the important events than the quarterly rates. Of women diagnosed with early breast cancer in each month, the percentage of them receiving BCS would be the monthly rate.

The analysis focused on the effect of period and its relationship to the 'diffusion process'. There is also an underlying assumption of the existence of a diffusion process or time trend. This implies the statistical estimation and testing of interest surrounds the α_i and β_i . Specifically, the β_i corresponds to the trend or slope effects. The α_i represents intercepts in the model. Our analysis will begin by testing equality of the β_i 's. To assess the effect of the events, we tested the significance of the shifts in predicted percentages of BCS between each of the neighboring time periods, that is,

the increase or decrease between the last month of one period and the first month of the other period. The P value of less than 0.05 was chosen as the statistical significance level. Computations were performed using SAS program [33].

Results

Characteristics of patients with breast cancer diagnosed in different time periods of events

Table 1 presents the distribution of some patient/tumor characteristics in women diagnosed with early stage breast cancer in four different time periods, such as age, race, marital status and tumor stage. In each time period, proportion of women in different age categories was similar. The largest shift was in the local tumor stage. White women had a slight decrease while there was a small increase in women of other races. The proportion of women was similar in those with different marital status.

Percentage of BCS in each time period by various factors

Table 2 shows the percentage of BCS performed in each time period. There was an increase over time in BCS particularly after 1991. The percentages of BCS doubled from 1983 to 1995 in both local and regional stage breast cancer. In addition, the percentages increased substantially in all age groups, especially in women aged 45–74. A similar increase appears in women with different race and marital status.

Figure 1 represent the trend in BCS in women with early stage breast cancer by months of the year, showing a gradual increase from early 1983 through 1984. By the second quarter of 1985, BCS rates increased sharply. Then the rates remained stable for some time at around 26%. However, at the third quarter of 1987 the rate suddenly dropped to below 22%. It took almost 8 months for the rates to get back to the 26% level. From then on, the use of BCS increased gradually to 1995 without obvious fluctuations.

Association between time and BCS by period

A regression model was estimated for 156 months after 1 January 1983. This model had a separate intercept and slope term for each of the four time periods and included the covariates which describe the characteristics of the breast cancer patients. The estimated

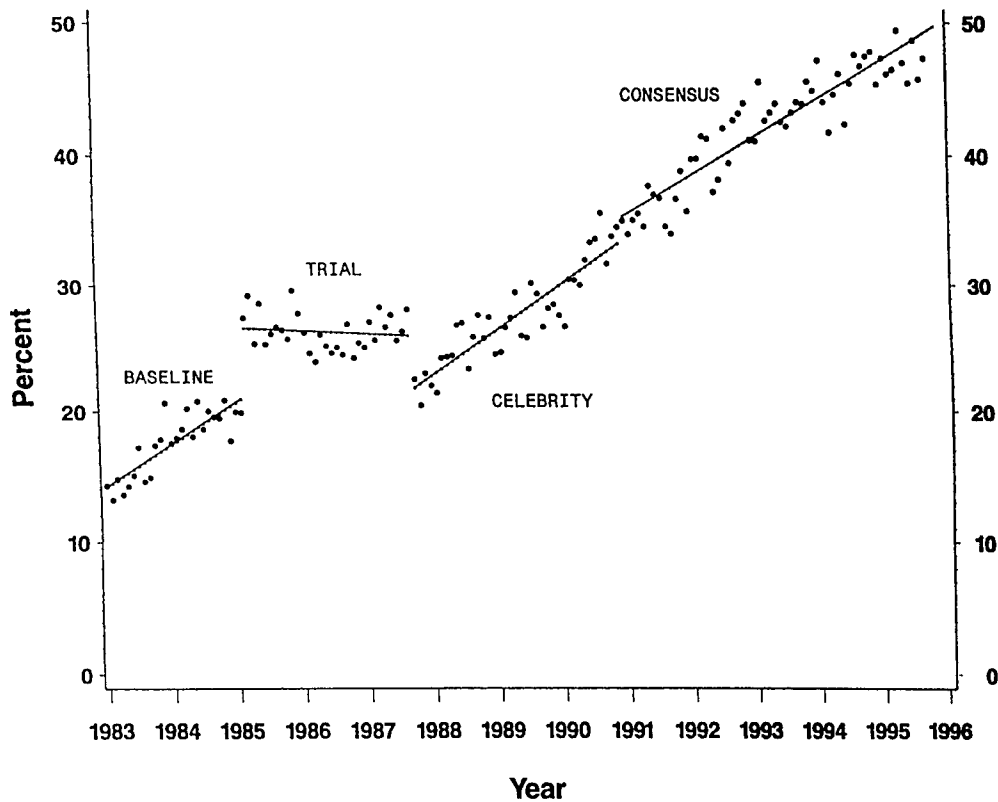


Figure 1. Monthly percentages in the use of breast conserving surgery in women with early stage breast cancer from 1983 to 1995. The dots represent the monthly percentage of women receiving breast conserving surgery (BCS) from 1983 through 1995, and the lines are the predicted percentage of women receiving BCS for each of the four periods (baseline, trial, celebrity and consensus).

Table 3. Results from the linear regression model for intercepts and slopes in each time period*

Parameters	Beta	95% Confidence interval	P-value (significance from zero)
Intercepts			
Baseline period	8.08	6.76-9.39	<0.001
Trial period	20.94	18.52-23.37	<0.001
Celebrity period	-1.40	-4.32-1.52	0.348
Consensus period	4.53	2.07-6.97	<0.001
Slopes			
Baseline period	0.25	0.17-0.33	<0.001
Trial period	-0.03	-0.09-0.02	0.247
Celebrity period	0.28	0.24-0.32	<0.001
Consensus period	0.24	0.22-0.26	<0.001

*Adjusted in the regression model for age (<65, 65-74, ≥75 years), race (white, non-white), marital status (married, unmarried), tumor stage (local, regional), and SEER areas (9 areas).

intercepts and slopes were shown in Table 3. For the baseline, celebrity and consensus periods, the slopes

indicated increasing use of BCS. The rate of increase varied between 0.24% and 0.28% per month. The slopes for these three periods were not statistically different from each other ($p = 0.120$). In contrast, there was no change over time in the use of BCS during the trial period ($p = 0.247$). We also tested the magnitude of the discontinuity between periods, and the effects were shown in lines in Figure 1. At the end of the baseline period there was an increase in BCS of 5.54% ($p < 0.001$). At the beginning of the celebrity period there was a decline of 3.55% ($p < 0.001$), while at the beginning on the consensus period there was a small but significant increase of 2.37% ($p < 0.001$). These findings were similar across nine SEER areas as well as for both local and regional tumor stages.

Discussion

Since the beginning of this century, the treatment of breast cancer has gone through some fundamental reforms, from Halsted radical mastectomy to modified

radical mastectomy, and then to BCS [1–3, 34–36]. In the 1960s and 1970s, there were scattered reports on the study of BCS [7, 37–40]. The rate of mastectomy started to decrease in 1974 [35]. However, the percentage of BCS remained very low [7, 41]. At that time, observational studies and controlled trials were scarce and the results were inconclusive [34–40]. In 1973, a large clinical trial was initiated in Milan and the results were first published in 1981, documenting the equivalent survival and recurrence advantages of the BCS plus radiation as compared to mastectomy [1]. However, this trial was only conducted in breast cancer patients with early stage tumors less than 2 cm and without palpable axillary nodes, and its results were not generalizable to breast cancer with larger tumor sizes. In 1983 the use of BCS was still low at 14%, but it increased gradually to 20% in the first quarter of 1985.

Within a matter of weeks in 1985 the use of BCS jumped from 20% in February to 27% in March, soon after the results of the first large scale US clinical trial were published in March. This sudden increase, which was shown among patients with different characteristics, was likely to be associated with the publication of this large trial in the US [3] and related media coverage [4, 5]. This large trial confirmed that BCS plus radiation provided equivalent outcomes in terms of survival and recurrence while preserving the breast [3, 20] and gaining a better quality of life [9, 42]. Our analysis has demonstrated a significant discontinuity in trends pre- and post-large clinical trial, and this supports the notion that well-conducted large clinical trial does seem to influence medical care.

From that time the percentage of BCS did not continue to increase but rather stayed at approximately 26% between March 1985 and September 1987. During the acceptance of a new technology into the community to replace an equally efficacious treatment (mastectomy), there may have been some mixed beliefs among physicians, some of whom were non-believers in BCS [43]. The surgeon's or physician's belief in the choice of BCS has been shown to be more important than patient's preference [43]. The full acceptance of new technology takes time and may need continuous intervention from professional publications and media. However, between 1985 and 1987, publications regarding BCS were scarce in the US.

The sudden 20% drop in the use of BCS within one month from September to October 1987 following the Nancy Reagan's choice of mastectomy, suggests

that the celebrity role model can influence clinical decisions [29]. The reduction in BCS was more substantial among persons with lower income and educational status [29]. While this effect was substantial, it was somewhat transient. It took only 8 months for the percentage of BCS to return to the original level at about 26%. Interestingly, because her tumor was just a quarter inch in diameter and noninvasive, Mrs. Reagan could have been an ideal candidate for BCS [4, 5, 44].

In the late 1980s and in the early 1990s, numerous publications provided scientific justification and essential evidence [13–19, 42–53] which lead the NIH to convene the consensus development conference [20]. While the consensus was to recommend BCS with radiation, it did not stimulate a dramatic jump in the use of BCS. There could be a number of reasons for this. The medical scientists involved in studies and individual physicians who treat cancer patients are considered to be the major players in the development and diffusion of medical innovations [54]. Most of this group was likely well-informed about BCS and already adjusting their practice behaviors to those the NIH recommended. Physician's awareness of the conference statement guidelines and their self-report of compliance may be high but their actual practice compliance may not be [24]. Although the conference was designed to facilitate sharing of updated biomedical research findings and spread knowledge of options and alternatives, the dissemination of conference results and other related findings takes considerable time to move through multiple channels into public knowledge. The increasing use of mammography since the mid 1980s could have made the tumor stage to shift toward local stages [55], therefore, increasing the number of candidates suitable for BCS.

A series of debates and publications before, during and after the conference probably played a key role in the gradual increase in BCS. The NIH conference statement did not specify the desired percentage of BCS; it only recommended that BCS be used for the 'majority' of women with early stage breast cancer [20]. If indeed 'majority' means over 50%, then the recommended rate of BCS was reached in November 1995. In that case, the NIH consensus conference and consensus statement could be termed a necessary intervention during the period of disseminating technology to the medical community and to the public as a whole to maintain the increase in the use of BCS. These patterns of distributing information are consistent with the diffusion theory, by which new

technology information spreads over many years to physicians and patients themselves through multiple channels [56].

However, the effects of this series of events on the time trend in the receipt of radiation therapy did not reflect the same pattern of changes seen for BCS. The trend for radiation therapy was smooth with a minimum increase from 1983 to 1995 (data not shown) [57, 58]. This might be because of the nature of the therapy. Radiation therapists depend on physicians to refer patients to them for treatment, which is often received daily for six weeks. The level of technology required for radiation therapy often requires a major commitment by hospitals [54] to purchase and maintain equipment, and this factor is usually under control of hospital administration rather than the physicians who might prescribe it. Therefore, BCS technology could be diffused more quickly because it does not require additional surgical equipment as compared to the traditional modified radical mastectomy.

There are several limitations to the findings in this study. During the late 1980s and the early 1990s, there were many cancer prevention control initiatives and women's health advocates who had an influence on women's attitudes toward their health as well as changes in insurance coverage for breast health care. These many factors may have contributed to an increase in the BCS rates, and so did the increasing use of mammography screening. However, none of these factors was as dramatic as those three critical events in the breast cancer history discussed in this study. Second, we only studied the population in SEER areas, which may not be representative of the entire US population [59]. It is unknown whether the effect of those events on the use of BCS would be the same or similar in other areas. The third important limitation is the difficulty of controlling for patient factors that led to the selection of a specific treatment, particularly comorbidity, functional status and individual preferences. We were also unable to assess the use of other therapies such as adjuvant chemotherapy and hormonal therapy as there was no reliable information of such therapies from SEER. However, these therapies were usually used either for prevention or for adjuvant treatment for women with local or regional stage breast cancer, therefore they may not have affected the rate of surgical treatment.

In conclusion, the use of BCS was significantly affected by the reports of a large scale US clinical trial of BCS and by celebrity action. These effects were

remarkable but transient. The NIH consensus statement only stimulated a small change in the use of BCS and may have played an important role, together with other cancer control initiatives, in maintaining the increasing trend in the use of BCS since the 1990s.

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Accuracy and Completeness of Medicare Claims Data for Surgical Treatment of Breast Cancer

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BACKGROUND. Although a number of studies have used Medicare claims data to study trends and variations in breast cancer treatment, the accuracy and completeness of information on surgical treatment for breast cancer in the Medicare data have not been validated.

OBJECTIVES. This study assessed the accuracy and completeness of Medicare claims data for breast cancer surgery to determine whether Medicare claims can serve as a source of data to augment information collected by cancer registries.

METHODS. We used the Surveillance, Epidemiology and End Results (SEER) Cancer Registry-Medicare data and compared Medicare claims on surgery with the surgery recorded by the SEER registries for 23,709 women diagnosed with breast cancer at ≥ 65 years of age from 1991 through 1993.

RESULTS. More than 95% of women having mastectomies according to the Medicare data were confirmed by SEER. For breast-

conserving surgery, 91% of cases were confirmed by SEER. The Medicare physician services claims and inpatient claims were approximately equal in accuracy on type of surgery. The Medicare outpatient claims were less accurate for breast-conserving surgery. In terms of completeness, when the 3 claims sources were combined, 94% of patients receiving breast cancer surgery according to SEER were identified by Medicare.

CONCLUSIONS. The combined Medicare claims database, which includes the inpatient, outpatient, and physician service claims, provides valid information on surgical treatment among women known to have breast cancer. The claims are a rich source of data to augment the information collected by tumor registries and provide information that can be used to follow long-term outcomes of Medicare beneficiaries.

Key words: breast cancer; mastectomy; breast conserving surgery; SEER; Medicare. (Med Care 2000;38:719-727)

Administrative databases have been increasingly utilized in studies of health care outcomes over the past decade.¹⁻⁸ For example, Medicare claims data have been used to estimate the incidence of breast

cancer,⁴⁻⁷ to examine treatment patterns for breast cancer,^{8,9} and to study clinical surveillance of breast cancer, such as postoperative use of radiotherapy.^{10,11} Although Medicare claims data have been found to

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be useful for research, there are some concerns, including the accuracy of the diagnostic and procedure coding,^{1-6,12} demographic coding errors,^{2,11} incomplete coverage of all Medicare beneficiaries,^{2,12} and completeness of the claims.^{2,11,13} Recently, Cooper and colleagues¹⁴ found that the sensitivity of Medicare data for detection of breast cancer was reasonably high, especially if Medicare parts A and B are combined and surgical procedure codes were used. On the other hand, Warren et al¹⁵ determined that the diagnostic codes from Medicare hospital claims had high predictive value for breast cancer incidence but that the diagnoses from the physician claims had low predictive value. Medicare data also have limited utility for measuring cancer stage.¹⁶

The accuracy and completeness of information on surgical treatment for breast cancer in Medicare data, however, have not been validated, even though a number of studies have used Medicare claims data to study trends and variations in breast cancer treatment.^{8-11,17} Although the coding and completeness of mastectomies in the inpatient claims appear to be very good,^{12,18} the accuracy and completeness of information on breast-conserving surgery (BCS) are not known. In particular, the increasing use of BCS^{8,19} and the shift to more outpatient treatment²⁰ have raised questions about the completeness and accuracy of claims for surgery performed outside the hospital.

This study was conducted to assess the accuracy and completeness of Medicare data for breast cancer surgery through the use of all available Medicare claims sources: hospital inpatient, hospital outpatient, and physician services data. Of interest is the extent to which the claims provide information on breast cancer-related surgery in the first course of therapy and whether the type of surgery is confirmed by an external source of data. The overall goal is to determine, with the use of a cohort of women reported by cancer registries as having breast cancer, whether Medicare claims can serve as a source of data to augment information collected by cancer registries and be used to describe surgical treatment patterns in older women with breast cancer.

Methods

Data Sources

We used the merged Surveillance, Epidemiology and End Results (SEER)-Medicare database

for this analysis. The SEER program, supported by the National Cancer Institute, includes population-based tumor registries in selected geographic areas. In 1992, these areas included the metropolitan areas of San Francisco-Oakland, Detroit, Atlanta, and Seattle; Los Angeles County; the San Jose-Monterey area; and the states of Connecticut, Iowa, New Mexico, Utah, and Hawaii.²¹ These areas cover ~14% of the US population.²¹ The registries ascertain all newly diagnosed (incident) breast cancer cases from multiple reporting sources, such as hospitals, outpatient clinics, laboratories, private medical practitioners, nursing/convalescent homes/hospices, autopsy reports, and death certificates.^{13,22,23} Information includes tumor location, size, and histological type; such demographic characteristics as age, gender, race, and marital status; and types of treatment provided within 4 months of the date of diagnosis.²² In the case of surgery, SEER records the most invasive surgery.

The Medicare program is administered by the Health Care Financing Administration (HCFA). It covers hospital, physician, and other medical services for >97% of persons ≥ 65 years of age.^{13,23} The Medicare claims data used in the study included the following 3 files: (1) Medicare Provider Analysis and Review File, which contains inpatient hospital claims; (2) the Hospital Outpatient Standard Analytic File, which contains the claims for outpatient facility services; and (3) the 100% Physician/Supplier File, which contains the claims for physicians' and other medical services. These data were available for all beneficiaries starting in 1991. Therefore, we used all cases diagnosed between January 1, 1991, and December 31, 1993.

Cases reported by the SEER registries from 1973 to 1993 have been matched against Medicare's master enrollment file. Of persons ≥ 65 of age appearing in the SEER records, Medicare eligibility could be identified for 94%. The method of linking these data has been described elsewhere.^{13,20} For SEER cases found to be Medicare eligible, their claims are available through 1994.

Study Population

The study population consisted of all female patients diagnosed with breast cancer at ≥ 65 years of age between 1991 and 1993. Excluded were women who did not have full coverage of both Medicare parts A and B or who were members of

HMOs in the year of diagnosis because claims from these organizations may not be included in the HCFA databases. Also excluded were 61 patients whose month of diagnosis was unknown and 126 patients with no information from SEER on surgical treatment. This left 23,709 patients for analysis (8,022 in 1991, 8,056 in 1992, and 7,631 in 1993).

Variable Definitions

Breast Cancer-Directed Surgery In SEER, BCS was defined as segmental mastectomy, lumpectomy, quadrantectomy, tylectomy, wedge resection, nipple resection, excisional biopsy, or partial mastectomy unspecified, with or without dissection of axillary lymph nodes. Mastectomy was defined as subcutaneous, total (simple), modified radical, radical, or extended radical mastectomy.

In Medicare, BCS was defined with the following codes: ICD-9-CM²⁴ procedure codes 8521 (local excision), 8522 (quadrantectomy), or 8523 (subtotal mastectomy) or common procedure terminology²⁵ codes 19120 (local excision), 19160 (partial mastectomy), or 19162 (partial mastectomy with axillary dissection). Mastectomy was defined with the following codes: ICD-9-CM procedure codes 8541 to 8542 (simple mastectomy), 8543 to 8544 (modified radical), or 8545 to 8548 (radical) or a common procedure terminology code on a physician or outpatient claim of 19240 (modified radical), 19220 (radical), or 19180 (simple mastectomy).

Analyses

Medicare claims for surgical treatment were categorized into 3 groups: mastectomy, BCS, and no cancer-directed surgery. Women were considered to have received mastectomy if any of 3 Medicare claim sources (inpatient, outpatient, or physician/supplier claims) indicated so, regardless of whether or not they had any claims for BCS. If they had claims for BCS only, they were defined as having received BCS. If they had neither claims for mastectomy nor for BCS, they were considered to have no cancer-directed surgery.

Because SEER collects only information on treatment within 4 months of the date of diagnosis,²³ we examined all Medicare claims from 1991

to 1994 for surgery that were made within 4 months (122 days) of the date of diagnosis. Because SEER reported only the month and year of diagnosis, we therefore arbitrarily defined the day of diagnosis in SEER as the 15th of the month. Date of surgery was determined from the claims source that first identified the type of surgery (mastectomy or BCS). For inpatient claims, it was defined as the date of admission. For outpatient and physician claims, it was defined as the earliest date of service.

Patient and tumor characteristics, such as age, race, tumor stage, and geographic areas, are available from the SEER data. The simple κ statistic was calculated to quantify the degree of agreement in surgical treatment categories between the 2 databases.²⁶ The odds ratios of concordance on surgical treatment between the 2 databases were generated from multivariate logistic regression analyses. These analyses adjusted for age, race, tumor stage, and geographic area because previous studies have found that the degree of agreement of information on treatment is affected by these factors.^{8,9,11,12,20} Four metropolitan areas (San Francisco–Oakland was combined with Los Angeles County and the San Jose–Monterey area in California) and 5 states, forming 9 areas, were adjusted in the analysis. All computer programming and analyses were completed with the SAS system.²⁷

Results

Table 1 presents comparisons of surgical treatment between the SEER and Medicare databases in women with breast cancer diagnosed from 1991 through 1993. Of 13,431 women having mastectomies according to the Medicare data, 95% were confirmed by SEER. For BCS, 88% of cases were confirmed by SEER. The simple κ statistic for overall agreement on surgery between SEER and Medicare was 0.75 (95% confidence interval [CI] 0.74 to 0.76). From Table 1, of the 23,709 total patients with breast cancer, in 21,299 (90%) there was information regarding surgical treatment in both SEER and Medicare. Among these patients, concordance between the 2 databases was 94%, and the κ statistic was 0.86 (95% CI 0.85 to 0.87). There was no statistically significant difference for the concordance rates between SEER and Medicare for cases diagnosed in 1991 compared with 1992 (χ^2 test, $P > 0.2$) or 1993 ($P > 0.09$).

TABLE 1. Comparison of Surgical Treatment Between SEER and Medicare Claims Made Within 4 Months of Date of Diagnosis for Women With Breast Cancer Diagnosed From 1991 to 1993

SEER	Medicare*			Total Row, n (%)
	No Cancer-Directed Surgery, n (%)	BCS, n (%)	Mastectomy, n (%)	
No cancer-directed surgery	674 (66.1) (32.6)	258 (25.3) (3.1)	87 (8.5) (0.7)	1,019 (100.0)
BCS	477 (5.7) (23.1)	7,231 (86.4) (88.0)	658 (7.9) (4.9)	8,366 (100.0)
Mastectomy	914 (6.4) (44.3)	724 (5.1) (8.8)	12,686 (88.6) (94.5)	14,324 (100.0)
Total column, n (%)	2,065 (100.0)	8,213 (100.0)	13,431 (100.0)	23,709

*Claims for surgical treatment were identified from the hospital inpatient, hospital outpatient, or physician services files in the Medicare database, and only those claims for surgery made within 4 months of the date of diagnosis of breast cancer were counted here. Women were considered to have received mastectomies if any of the 3 Medicare claim sources (inpatient, outpatient, or physician claims) indicated so, regardless of whether or not they had any claims for BCS. If they had claims for BCS only, they were defined as having received BCS. If they had no claims for mastectomy or BCS, they were considered to have no cancer-directed surgery. Values are n (row %) followed by column percent.

Table 2 presents data on the accuracy of information on type of surgery in each of the 3 Medicare claims sources compared with SEER. In these analyses, we limited the analyses to cases in which information about type of surgery was available both in the particular Medicare claims source examined and in SEER. Approximately 96% of patients with mastectomy claims either in Medicare physician files or in Medicare inpatient files were confirmed by SEER. As for BCS, 91% and 88%, respectively, were confirmed by SEER. Of patients with mastectomies in Medicare outpatient files, 83% were confirmed by SEER, but only 50% of patients with BCS claims in outpatient files were confirmed by SEER. Overall agreement between Medicare and SEER was 95% for mastectomy and 91% for BCS (Table 2).

Table 3 presents the completeness of information on surgery from the different sources of Medicare claims compared with SEER. The Medicare physician services claims identified >91% of patients who received breast cancer surgery according to SEER. The Medicare inpatient claims identified 68%; the outpatient claims identified only 33%. As might be expected, the 3 sources of the Medicare claims data differed in their completeness, depending on the type of breast cancer surgery performed. The outpatient claims had data on surgery for 44% of those receiving BCS according to SEER but for only 27% of those receiving mastectomies (Table 3). The inpatient claims had data on 86% of those receiving mastectomies and

only 34% of those receiving BCS. The physician claims showed similar degrees of completeness of information on surgery for patients receiving mastectomies (91%) and BCS (91%). Of 13,341 patients with mastectomies and 8,213 with BCS, 54 (0.4%) of patients with mastectomies and 166 (2.0%) patients with BCS were identified by the outpatient claims and were not identified in either the inpatient or physician claims. When the 3 claims sources were combined, 94% of surgeries according to SEER were identified by Medicare.

Table 4 presents 3 different comparisons of information on receipt of surgery between the 2 databases. The percentage of patients in whom there is agreement on receipt of surgery is given, as is the κ statistic, as a function of patient and tumor characteristics. The last column was a multivariate analysis, showing the odds of a patient having concordant information regarding receipt of surgery between the 2 databases. Concordance between the 2 data sets was significantly greater in older women and in whites. Agreement on receipt of surgery was significantly better in those with local or regional stage but much lower in those with distant or unstaged compared to those with in situ cancer. There was variation among the 9 SEER areas in the extent of concordance on type of surgery between SEER and Medicare, ranging from 81% to 90% (data not shown). When the region variables were excluded from the logistic model, the magnitude of the odds ratios for other variables changed slightly, but the direction and

TABLE 2. Accuracy of Information on Type of Surgery in the Medicare Claims Database Compared With SEER

Source of Medicare Claims	Cases With Claims for Mastectomy in Medicare Files Confirmed by SEER, % (No. Identified by SEER/No. in Medicare)*	Cases With Claims for BCS in Medicare Files Confirmed by SEER, % (No. Identified by SEER/No. in Medicare)*
Medicare physician claims	96.2 (12,096/12,580)	87.9 (7,105/8,087)
Medicare inpatient claims	96.0 (12,087/12,586)	91.3 (2,369/2,596)
Medicare outpatient claims	82.8 (231/279)	49.7 (3,612/7,269)
Three Medicare claims combined [†]	95.1 (12,686/13,344)	90.9 (7,231/7,955)

*The analyses are restricted to those cases in which a surgical therapy is coded in both SEER and the particular Medicare database being assessed for accuracy. As a result, denominators varied by paired comparisons (including the combined numbers at the bottom of the table).

[†]If there was a claim for mastectomy in any of the 3 Medicare claims sources (hospital inpatient, hospital outpatient, or physician claims files), the case was categorized as mastectomy. Otherwise, the case was categorized as BCS. Only claims for surgery made within 4 months of the date of diagnosis of breast cancer were examined to ascertain surgery status.

significance of the odds ratios remained unchanged.

Discussion

The question addressed by this study is whether the Medicare claims data provide valid information on surgical treatment for patients known to have breast cancer. This question has 2 components: one involves accuracy and the other is completeness. We examined these issues for each of the 3 sources of Medicare claims and for the combined data from all 3 sources. When we were

addressing these issues, we used the SEER data as the reference group because the SEER program of the National Cancer Institute is the most authoritative source of data on cancer incidence, mortality, and treatment.^{28,29} SEER was designed primarily to provide such information,²¹ whereas the Medicare claims data are administrative in nature and not designed for research purposes.^{1-6,11-13} In addition, the validation study showed that the results on breast cancer surgery were similar in SEER compared with the National Cancer Database of the American College of Surgeons Commission on Cancer and the American Cancer

TABLE 3. Completeness of Medicare Claims on Surgery (Mastectomy or BCS) for Women With Breast Cancer Diagnosed From 1991 Through 1993

Source of Medicare Claims	Patients With Mastectomy According to SEER Who Were Identified by Medicare Claims as Having Any Surgery* (n = 14,324), n (%)	Patients With BCS According to SEER Who Were Identified by Medicare Claims as Having Any Surgery* (n = 8,366), n (%)	Patients With Either Mastectomy or BCS According to SEER Who Were Identified by Medicare Claims as Having Any Surgery (n = 22,690), n (%)
Physician claims	13,078 (91.3)	7,589 (90.7)	20,667 (91.1)
Inpatient claims	12,314 (86.0)	2,868 (34.3)	15,182 (67.9)
Outpatient claims	3,888 (27.1)	3,660 (43.7)	7,548 (33.2)
3 Claims combined [†]	13,410 (93.6)	7,889 (94.3)	21,299 (93.9)

*Surgery includes either mastectomy or BCS.

[†]Medicare claims for surgery were identified from the hospital inpatient, hospital outpatient, or physician services files. Only claims for surgery made within 4 months of the date of diagnosis of breast cancer were examined to ascertain breast cancer surgery. If there was a claim for mastectomy in any of the claims sources, the case was categorized as mastectomy. Otherwise, the case was categorized as BCS.

TABLE 4. Comparison of Surgical Treatment Between SEER and Medicare in Women With Breast Cancer Diagnosed From 1991 Through 1993

Characteristics From SEER Registry	Number of Patients	Medicare Versus SEER		
		Simple κ (95% CI)	Concordant Cases, %	Adjusted Odds Ratio of Being Concordant (95% CI)*
All patients	23,709	0.75 (0.74–0.76)	86.8	...
Age, y				
65–74	12,902	0.71 (0.70–0.72)	84.8	1
75–84	8,408	0.79 (0.78–0.80)	88.9	1.39 (1.27–1.52)
85+	2,399	0.84 (0.82–0.86)	90.5	1.51 (1.30–1.76)
Race				
White	21,534	0.75 (0.74–0.76)	87.0	1
Black	1,342	0.73 (0.70–0.76)	84.1	0.79 (0.67–0.94)
Other	833	0.77 (0.73–0.81)	87.2	1.17 (0.90–1.53)
Cancer stage				
In situ	2,176	0.74 (0.71–0.76)	86.0	1
Local	13,546	0.77 (0.76–0.78)	88.3	1.26 (1.09–1.45)
Regional	5,051	0.70 (0.68–0.73)	88.8	1.44 (1.23–1.69)
Distant	914	0.58 (0.53–0.62)	71.8	0.39 (0.32–0.48)
Unstaged	2,022	0.68 (0.65–0.70)	79.6	0.56 (0.47–0.68)

*Odds ratios were derived from the logistic regression model, adjusted for the variables listed in the table and 9 SEER areas.

Society.³⁰ They found that 53.4% of women with breast cancer had mastectomies and 37.7% had BCS in SEER compared with 54.1% and 40.7%, respectively, in the National Cancer Database.³⁰

In terms of accuracy, among patients for whom information on type of surgery was available from both Medicare and SEER, 95% of patients who received mastectomies according to the combined Medicare claims were confirmed by SEER. Of those who received BCS, 91% were confirmed by SEER. The Medicare physician services claims and inpatient claims were approximately equal in accuracy for type of surgery. The Medicare outpatient claims were less accurate for BCS. The concordance is greater in older women (≥ 75 years) and in patients with local or regional stage cancer but varies among the SEER areas.

The accuracy of Medicare data on breast cancer surgery has also been studied with different reference groups, such as reabstracted records or local cancer registry data. Fisher et al¹² compared Medicare inpatient hospitalization codes for mastectomy with that identified from the reabstracted hospital record. Of those mastectomies identified by the reabstracted record, 97% were found to have a code for mastectomy in Medicare data. However, only 33 cases were reviewed. In another study, discharge data from one hospital in New York City were compared with hospital cancer

registry data. The study found a high concordance rate for mastectomy between the 2 databases.¹⁸ Warren et al²⁰ described a comparison of mastectomy between Medicare and SEER in patients who underwent mastectomies only in 1992–1993. The agreement rate was 95% for inpatients and 89% for outpatients.²⁰ These previous studies on breast cancer surgery depended on the Medicare inpatient or outpatient claims data but did not use the physician claims data. We found in this study that information on surgery identified from the physician service claims was similar in accuracy compared with that from the inpatient claims. Only 50% of BCS from the outpatient claims could be identified by SEER. This may largely reflect clinical practice patterns because many women who had BCS in the outpatient settings for diagnostic purposes may end up with a mastectomy in hospitals. Therefore, the combined data from all 3 sources of Medicare claims should generate the most accurate information on surgery.

We also found that any single Medicare claims source did not provide complete information on surgery (Table 3), although Medicare physician claims seemed the most complete among the 3 Medicare claims sources. Medicare outpatient claims, although least complete, still identified 0.4% of patients with mastectomies and 2.0% of cases with BCS that otherwise were not identified

by either inpatient or physician claims. When the 3 claims sources were combined, 94% of patients receiving breast cancer surgery according to SEER were identified by Medicare.

A number of factors might have contributed to reduce the completeness of the Medicare data on surgery. First, information on surgery from Medicare was restricted to those who had claims within 4 months of the date of diagnosis. This made it compatible with SEER data because SEER collects information only within this period.²³ However, this might have excluded those who had late claims for surgery and thus underestimate the degree of agreement between 2 data sets. We did additional analyses extending the time frame from 4 to 12 months after diagnosis. As a result, the overall agreement between SEER and Medicare on type of surgery improved ($\kappa=0.78$ compared with 0.75 in Table 1). Second, younger patients who recently became eligible for Medicare coverage might have less complete information in Medicare claims records. Indeed, younger age was a risk factor for lack of concordance between Medicare and SEER (Table 4). Third, if patients switched their care to HMOs or received care in Veterans Affairs hospitals, they may have missing information in the Medicare claims. Finally, it may be possible that a very small proportion of patients in SEER were mismatched with the Medicare data. If this happened, those patients would not have had Medicare claims for breast cancer surgery.

As previous studies also showed, Medicare claims data on the validity of mastectomy¹² have been found to have a high level of accuracy. In this study, we demonstrated that information on mastectomy and BCS is reasonably accurate and complete for women known to have breast cancer. Hence, using Medicare claims data may overcome the limitations in ascertaining treatment from cancer registries.

This study has some limitations. First, this analysis used only the Medicare claims for women identified from the SEER data as having cancer. The accuracy and completeness of breast cancer-related procedures for non-SEER cases are unknown. It is important to note that the presence of a Medicare claim with a breast cancer-related procedure does not confirm that the woman had cancer because some procedures, such as BCS, may be used for diagnostic as well as therapeutic purposes. Second, we used the SEER data as the reference group. Although SEER provides valid information on breast cancer surgical treatment,³⁰ we found a number of women with

breast cancer who received cancer-directed surgery according to the Medicare claims data that were not recorded in the SEER data. For example, of 1,019 patients who did not have surgery according to SEER, 345 (34%) had claims for such a surgery in Medicare (Table 1). As previous investigators^{11,23,31} also demonstrated, SEER might not provide complete information on treatment because it might sometimes miss information from outpatient settings and might not record those who moved immediately after diagnosis or underwent treatment in an out-of-state facility.³² Furthermore, this study was performed in a cohort of women who were diagnosed with breast cancer and were successfully linked with Medicare data (94% match rate).¹³ Also excluded were patients enrolled in HMOs and those without coverage of both Medicare parts A and B in 1991–1993. It is unknown whether the 2 databases would agree on type of surgery for those cases excluded, particularly those that were not ascertained by SEER as breast cancer but identified by Medicare data alone. Nevertheless, there was no external validation of the information on receipt of surgical treatment to assess the accuracy of the Medicare and SEER data sources and to determine which data source is "correct." This may be achieved by reviewing the medical records for a sample of patients with breast cancer. However, all patient identifiers were removed from the final SEER-Medicare linked database for confidentiality reasons, precluding these analyses.

In conclusion, the combined Medicare claims database, which includes the inpatient, outpatient, and physician service claims, provides valid information on surgical treatment among women known to have breast cancer. The claims are a rich source of data to augment the information routinely collected by tumor registries. In particular, it provides information on receipt of medical services that can be used to examine patterns of care and follow long-term outcomes of Medicare beneficiaries.

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program tumor registries in the creation of the SEER-Medicare Database.

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Patterns of Use of Chemotherapy for Breast Cancer in Older Women: Findings From Medicare Claims Data

By Xianglin Du and James S. Goodwin

Purpose: There is little population-based information available on the use of chemotherapy in women with breast cancer. This study describes the use of chemotherapy through analysis of Medicare claims and determines the correlates of chemotherapy use.

Patients and Methods: We used the merged Surveillance, Epidemiology, and End Results-Medicare database and identified women ≥ 65 years of age diagnosed with breast cancer in 1991 and 1992. Chemotherapy was ascertained from Medicare claims through procedure codes for chemotherapy made within 24 months of the diagnosis.

Results: In women with stages I, II, III, and IV breast cancer, the percentage receiving chemotherapy within 24 months of diagnosis was 5.1%, 19.5%, 33.9%, and 35.2%, respectively. Most women receiving chemotherapy had two to 12 claims; the median number was eight. Use of chemotherapy decreased significantly

with age across all tumor stages; eg, in women with stage III cancer, the use of chemotherapy declined from 49% in those aged 65 to 69 years to 10% in those ≥ 80 years old. In a multivariate analysis, there was little variation by ethnicity. Chemotherapy use was highest (70%) in women aged 65 to 69 years with node-positive and estrogen receptor-negative tumors and lowest (5%) in those with node-negative and estrogen receptor-positive tumors. Compared with those without comorbid diseases, patients with a comorbidity score of 2 had significantly lower use of chemotherapy.

Conclusion: Medicare claims data seem to provide valuable information on the use of chemotherapy for breast cancer in older women. However, external validation of the accuracy and completeness of these data is required before any firm conclusion can be drawn.

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META-ANALYSES OF 47 randomized clinical trials of chemotherapy involving 19,000 women with early-stage breast cancer demonstrated a significant improvement in both recurrence-free and overall survival.^{1,2} For example, in women with cancer localized to the breast, chemotherapy produced an absolute improvement of 7% to 11% in 10-year survival for those younger than 50 years of age and of 2% to 3% for those 50 to 69 years of age.² Because of its proven efficacy, chemotherapy is recommended to be offered to all premenopausal women with stage II or higher stage breast cancer and to premenopausal and postmenopausal women with estrogen receptor-negative tumors greater than 1 cm in size regardless of lymph node status.³⁻⁸ Because few data are available on the efficacy of chemotherapy in women ≥ 70 years old,^{1,2} recommendations on chemotherapy use in this population are not as clear cut; most authorities stress the need for making a decision based on the particular condition of the individual patient.³⁻⁵

Little information is available on the actual use of chemotherapy in the community.⁹⁻¹⁹ In a pilot study initiated by the National Cancer Institute and conducted in 17 hospitals, the use of chemotherapy in women 65 to 74 years of age with breast cancer was 4% for local stage, 55% for regional stage, and 49% for distant stage.⁹ In a national, hospital-based survey of patterns of care for breast cancer conducted by the Commission on Cancer of the American College of Surgeons, 47% of women with breast cancer of all ages (median age, 64 years) used either chemotherapy or

tamoxifen in 1990,¹⁰ but the stage-specific rate of chemotherapy in this report was not given. A hospital-based study in Massachusetts and Minnesota showed that 94% to 97% of younger premenopausal women with positive lymph nodes received chemotherapy.¹⁹ In a medical record review for women ≥ 65 years of age with breast cancer diagnosed in a large health maintenance organization (HMO), the use of chemotherapy was 13%.¹² Other studies showed that the receipt of chemotherapy decreased with age.¹⁴⁻¹⁸ The data are scarce on the use of chemotherapy from population-based studies. The Surveillance, Epidemiology, and End Results (SEER) program, a national, population-based cancer registry, no longer reports data on chemotherapy because of concerns about completeness.^{20,21} Therefore, this study aims to use the SEER-Medicare linked data to

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describe the use of chemotherapy through analysis of Medicare claims and to determine the correlates of chemotherapy use.

PATIENTS AND METHODS

Data Sources

We used the merged SEER-Medicare database for this analysis. The SEER program, supported by the National Cancer Institute, includes population-based tumor registries in selected geographic areas: the metropolitan areas of San Francisco/Oakland, Detroit, Atlanta, and Seattle; Los Angeles county; the San Jose-Monterey area; and the states of Connecticut, Iowa, New Mexico, Utah, and Hawaii.²² These areas cover approximately 14% of the United States population.²² The registries ascertain all newly diagnosed (incident) breast cancer cases from multiple reporting sources such as hospitals; outpatient clinics; laboratories; private medical practitioners; nursing homes, convalescent homes, and hospices; and autopsy reports and death certificates.²³ Information includes tumor location, size, American Joint Committee on Cancer stage, axillary node status, and estrogen receptor status; demographic characteristics such as age, sex, race, and marital status; and types of treatment provided within 4 months after the date of diagnosis.²³

The Medicare Program is administered by the Health Care Financing Administration (HCFA). The program covers hospital, physician, and other medical services for more than 97% of persons ≥ 65 years of age.²¹ The Medicare claims data used in the study included the following three files:²⁴ (1) Medicare Provider Analysis and Review file, which contains inpatient hospital claims; (2) the Hospital Outpatient Standard Analytic File, which contains the claims for outpatient facility services; and (3) the 100% Physician/Supplier file, which contains the claims for physicians and other professional services. These data are available for all beneficiaries starting in 1991, and their Medicare claims are available through 1994. To allow 2 years of Medicare claims for chemotherapy after diagnosis, we identified cases diagnosed in 1991 and 1992.

Cases reported by the SEER registries from 1973 to 1993 have been matched against Medicare's master enrollment file. Of persons ≥ 65 years of age appearing in the SEER records, Medicare eligibility could be identified for 94% of these cases. The method of linking these data has been described by Potosky et al.²¹

Study Population

The study population consisted of all female patients ≥ 65 years of age who were diagnosed with breast cancer in 1991 and 1992. Women who did not have full coverage of both Medicare Part A and Part B or who were members of HMOs were excluded because claims from these organizations may not be complete. Thus 10,604 patients with stages I to IV breast cancer were available for the analysis. Patient and tumor characteristics such as age, race, marital status, tumor stage, and geographic areas are available from the SEER data.

Chemotherapy

The procedures and revenue center codes for chemotherapy administration made within 24 months of diagnosis of breast cancer were assessed. These codes included the International Classification of Diseases (9th edition, clinical modification [ICD-9-CM]) procedure code of 9925 for a hospital inpatient or outpatient facility claim of chemotherapy (injection or infusion of cancer chemotherapeutic sub-

stance)²⁵; the common procedure terminology codes of 96400 to 96549, J9000 to J9999, and Q0083 to Q0085 for a physician or outpatient claim of chemotherapy administration^{26,27}; and the revenue center codes of 0331 (chemotherapy injected), 0332 (chemotherapy oral), and 0335 (chemotherapy intravenous) for an outpatient claim of chemotherapy.²⁸ The ICD-9-CM V codes²⁵ of V58.1, V66.2, or V67.2 for follow-up examination or care after chemotherapy were also used, which generated two additional cases in the category of receiving chemotherapy within 6 months of diagnosis.

Surgery and Radiation Therapy

In SEER, cancer-directed surgery was defined as either mastectomy (total, subcutaneous, radical, or modified radical mastectomy) or breast-conserving surgery (BCS)(segmental mastectomy, lumpectomy, quadrantectomy, tylectomy, wedge resection, nipple resection, excisional biopsy, or partial mastectomy unspecified). The radiation therapy included beam radiation, radioactive implants, radioisotopes, or other radiation as documented in SEER.²³

Comorbidity Index

Comorbidity was ascertained from Medicare claims data through diagnoses or procedures made 2 years before the diagnosis of breast cancer. We used the comorbidity index created by Charlson²⁹ and later validated by Romano et al using the ICD-9-CM diagnosis and procedure codes.³⁰ Both the Medicare inpatient and outpatient claims were searched for comorbid conditions not including breast cancer diagnosis codes (ICD-9-CM codes of 174x). Patients who had no inpatient or outpatient Medicare claims during this period were coded as a separate category.

Analyses

Because SEER reported only the month and year of diagnosis of breast cancer, we arbitrarily defined the day of diagnosis in SEER as the 15th of the month. For inpatient claims for chemotherapy, diagnosis was defined as the date of admission. For outpatient and physician claims, diagnosis was defined as the earliest date of service. Chemotherapy was defined if there was at least one claim for chemotherapy within specified time periods after diagnosis (6 months or 24 months).

The odds ratios of receiving chemotherapy in women with various patient and tumor characteristics were generated from multivariate logistic regression analyses. These analyses adjusted for age, race, marital status, tumor stage, tumor size, node status and estrogen-receptor status, and comorbidity indices, which are considered to likely affect the use of chemotherapy in women with breast cancer. All computer programming and analyses were completed using the SAS system (SAS Institute, Cary, NC).³¹

RESULTS

Table 1 presents how claims for chemotherapy were identified through the six types of codes in Medicare. According to the combined results from all six different types of codes in Medicare, 1,129 patients (10.6%) were identified as receiving chemotherapy within 6 months of diagnosis. Most cases were identified by both common procedure terminology codes and HCFA Coding System-J codes. Other codes also contributed to the completeness of the information on chemotherapy (Table 1). For example,

Table 1. Number of Women With Breast Cancer Diagnosed in 1991 and 1992 Who Could Be Identified as Having Received Chemotherapy*

Medicare Codes for Chemotherapy	Cases With Chemotherapy Identified by Each Code†		Cases for Which Chemotherapy Can Only Be Identified by Each of 6 Codes‡	
	No.	%	No.	%
CPT codes	949	84.1	64	5.7
HCPCS J codes	907	80.3	51	4.5
ICD-9-CM procedure codes	184	16.3	23	2.0
HCPCS Q codes	143	12.7	24	2.1
Revenue center codes	105	9.3	4	0.4
ICD-9-CM V codes	52	4.6	2	0.2
All above codes combined	1129	100.0		

Abbreviations: CPT, Common Procedure Terminology; HCPCS, HCFA Common Procedure Coding System; ICD-9-CM, International Classification of Diseases, 9th revision, Clinical Modification.

*Identified by different codes in Medicare claims data for claims made within 6 months of diagnosis.

†A patient receiving chemotherapy is frequently identified by two or more codes in Medicare.

‡Denotes cases that would otherwise be missed if only other five codes were used.

the revenue center codes identified four additional cases with receipt of chemotherapy that otherwise would have been missed if only the other five codes were used.

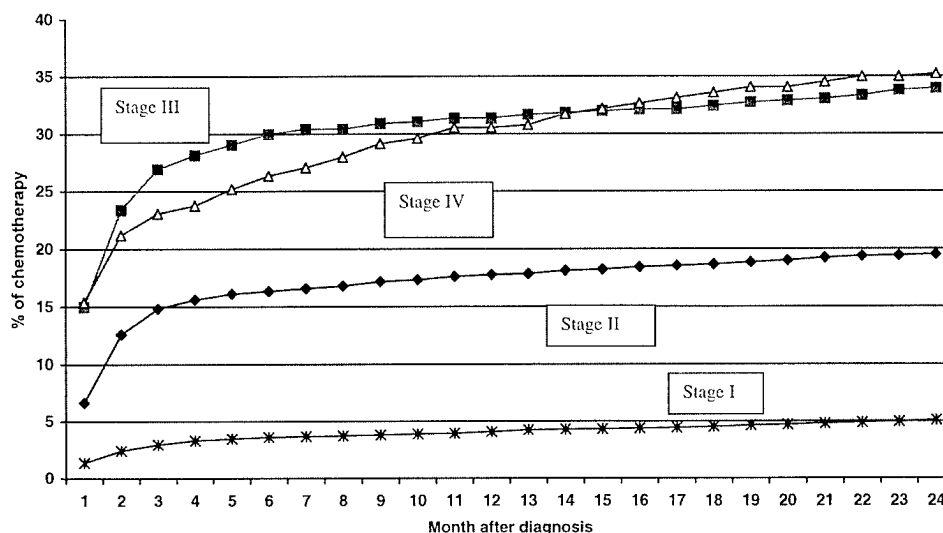
Figure 1 presents the cumulative percentage of claims for chemotherapy made within 24 months after diagnosis of breast cancer stratified by American Joint Committee on Cancer stage. In women with stage I, II, III, and IV breast cancer, the rate of chemotherapy within 6 months after diagnosis was 3.6%, 16.3%, 29.9%, and 26.3%, respectively, whereas the rate within 24 months after diagnosis was 5.1%, 19.5%, 33.9%, and 35.2% respectively. The overall rate of receipt of chemotherapy within 6 months of diagnosis among the 10,604 women diagnosed with stage I or higher breast cancer was 10.6%.

Figure 2 presents the number of claims for chemotherapy within 24 months of diagnosis for women with stages I, II,

III, and IV who had at least one claim for chemotherapy. Most women (67%) had between two and 12 claims, whereas 12% had one claim and 21% had more than 12 claims. The mean number of claims for chemotherapy was 10 (SD = 9.8, median = 8).

Table 2 presents the use of chemotherapy within 6 months of diagnosis stratified by patient characteristics and tumor stage. Use of chemotherapy decreased significantly with age across all tumor stages; for example, in women with stage III cancer, chemotherapy use decreased from 48% in those 65 to 69 years of age to 10% in those ≥ 80 years of age. There was little variation by ethnicity, while married women had higher rates of chemotherapy use in all stages. Higher percentages of women receiving no cancer-directed surgery or receiving mastectomy with radiation had chemotherapy.

Fig 1. Cumulative percentage by stage of women with breast cancer diagnosed in 1991 and 1992 who had claims for chemotherapy in Medicare submitted within 24 months after diagnosis of breast cancer.



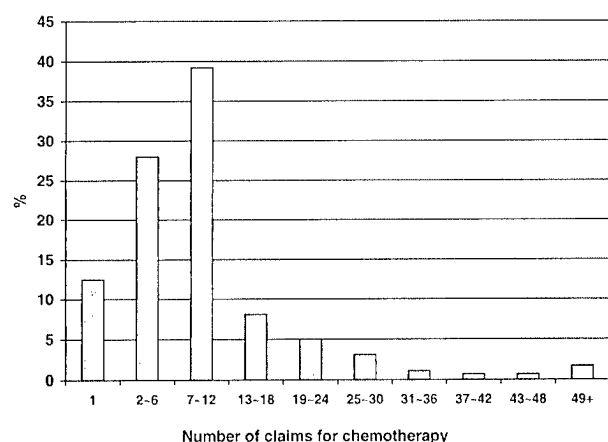


Fig 2. Number of claims for chemotherapy in Medicare within 24 months after diagnosis in women with stages I, II, III, and IV breast cancer. The mean number of claims for chemotherapy was 10 (SD = 9.8, median = 8).

Table 3 presents the percentages of women receiving chemotherapy by node and estrogen-receptor status. The data are presented for all women ≥ 65 years old and separately for women 65 to 69 years old. Women with node-positive and estrogen receptor-negative tumors had a very high rate of chemotherapy use, particularly in those women who were 65 to 69 years of age (70%). Women with node-negative and estrogen receptor-positive tumors had a much lower percentage of chemotherapy use.

Table 4 presents a multivariate analysis of the likelihood of receiving chemotherapy by simultaneously adjusting for factors presumed to affect such use. The use of chemotherapy significantly decreased with age. There was no significant difference in the use of chemotherapy among different ethnicities. Women with stage II, III, or IV tumors at diagnosis were more likely to receive chemotherapy than those with stage I tumors. Compared with women with a tumor size of less than 1 cm, those with larger tumors were more likely to receive chemotherapy. As expected, the use of chemotherapy was higher in women with node-positive tumors than those with negative nodes and higher in those with hormone receptor-negative tumors. Compared with those without comorbid diseases, patients with comorbidity scores of ≥ 1 had lower rates of chemotherapy use, but this was significant only for those with a comorbidity score of 2. There were no significant differences among women receiving other types of therapies (surgery and radiation), except that women who received BCS plus radiation were significantly less likely to have chemotherapy compared with those without cancer-directed surgery.

DISCUSSION

This study described the patterns of receipt of chemotherapy in older women with breast cancer using Medicare claims data. The overall percentage of chemotherapy use in women with stage I to IV breast cancer was 10.6%, with

Table 2. Receipt of Chemotherapy Within 6 Months After Diagnosis in Women With Breast Cancer in 1991 and 1992

Patient and Tumor Characteristics	Total		Women Receiving Chemotherapy by Stage (%)			
	No. of Cases	Women Receiving Chemotherapy (%)	Stage I (n = 5,824)	Stage II (n = 3,697)	Stage III (n = 654)	Stage IV (n = 429)
Age						
65-69 years	2,893	18.1	6.5	30.2	48.5	38.5
70-74 years	2,901	12.2	3.6	18.8	45.1	36.0
75-79 years	2,280	7.2	2.5	10.8	22.9	19.5
≥ 80 years	2,530	3.1	1.0	3.7	10.1	9.7
Race						
White	9,754	10.4	3.6	16.2	30.0	26.5
Black	540	14.1	5.1	17.6	28.6	26.8
Other	310	9.4	2.2	17.3	33.3	18.2
Marital status						
Married	4,368	12.9	4.2	21.7	37.4	37.4
Unmarried	5,937	9.0	3.2	12.9	26.2	20.7
Unknown	299	7.7	2.4	11.5	25.0	18.8
Other therapies*						
No surgery	291	24.4	5.6	9.7	29.0	27.2
BCS only	1,446	7.4	3.6	10.8	31.6	37.5
BCS and RT	2,236	6.9	3.2	15.6	29.4	23.1
Mastectomy only	6,131	10.8	3.8	16.7	27.2	19.4
Mastectomy and RT	500	27.2	9.1	24.3	36.8	30.2
Total	10,604	10.6	3.6	16.3	30.0	26.3

Abbreviation: RT, radiation therapy.

Table 3. Receipt of Chemotherapy Within 6 Months After Diagnosis in Older Women With Stages I to IV Breast Cancer in 1991 and 1992

Node and ER Status	All Women Aged 65 Years and Older		Women Aged 65-69 Years	
	No. of Cases	Women Receiving Chemotherapy (%)	No. of Cases	Women Receiving Chemotherapy (%)
Node-positive and ER-positive	1,741	20.9	509	31.6
Node-positive and ER-negative	335	48.4	123	69.9
Node-positive and ER unknown	418	23.0	115	45.2
Node-negative and ER-positive	3,879	2.9	1,134	4.8
Node-negative and ER-negative	689	18.7	255	26.3
Node-negative and ER unknown	1,319	3.6	395	6.6
Node not examined	2,223	9.6	362	21.6
Total	10,604	10.6	2,893	18.1

Abbreviation: ER, estrogen receptor.

greater use in stage III (30.0%) and stage IV (26.3%) than in stage II (16.3%). Women with estrogen receptor-negative tumors were more likely to receive chemotherapy. Use of chemotherapy decreased with patient age across all stages, and there was little variation by ethnicity.

There are several reasons to believe that Medicare claims data may produce valid information about receipt of chemotherapy. First, our findings were similar to other smaller community-based surveys of patterns of care for breast cancer in older women.^{12,13} For example, a community-based survey found that of 130 patients aged ≥ 65 years with newly diagnosed breast cancer in Philadelphia in 1993 to 1994, 13% used chemotherapy,¹² which is comparable to the overall rate of 10.6% found in our study. Second, the patterns of chemotherapy use would be expected. That is, chemotherapy use was higher in advanced stages, it increased in women with estrogen receptor-negative tumors, and it decreased markedly in women ≥ 70 years. The fact that women with stage IV were actually slightly less likely than women with stage III cancer to receive chemotherapy is consistent with reports in younger women.¹¹ Third, the distribution of total number of chemotherapy treatment received is comparable to current standard of care, which recommends four, six, or 12 cycles of chemotherapy depending on the specific agents used.^{3,4,32,33} The median number of claims for chemotherapy within 24 months after diagnosis was eight, with 67% of women receiving two to 12 treatments (Fig 2).

How complete is the information on chemotherapy in the Medicare claims? There are theoretical reasons to believe they might be complete. For example, the claims are directly tied to reimbursement for the provider and facility. In addition, other investigations into the validity of using Medicare data to identify the receipt of radiation therapy³⁴ and the type of surgery^{35,36} after the diagnosis of breast cancer have found them to be more than 92% complete when compared with SEER data. However, in this study, we

have no source of comparison to use as a gold standard, because SEER data are considered incomplete on chemotherapy.^{20,21} Indeed, information on chemotherapy is not even included in the SEER public use data set. Nevertheless, the fact that Medicare data demonstrate good validity in other aspects of breast cancer care (radiation therapy, BCS, and mastectomy)^{34,35} may provide indirect support for the validity of the information for chemotherapy in Medicare. However, there remain reasons for concern that the Medicare data may not be complete. Younger patients who recently became eligible for Medicare coverage at ages 65 to 66 years might have less complete information for Medicare claims records, because some who continue to work after age 65 (or who have a spouse who continues to work) may have employer-funded health benefits and may not immediately use Medicare.³⁴ In addition, if patients switched their care to HMOs or received care in Veterans Affairs hospitals after the year of their diagnosis, they may have missing information in the Medicare claims.³⁵ As previously demonstrated, Medicare data provide reasonably accurate and complete information on invasive surgeries.^{35,36} However, Medicare information on procedures other than invasive surgeries was found to be less accurate.³⁶

In the absence of an external standard of comparison, certain internal consistencies provide indirect evidence for both the accuracy and completeness of the Medicare data on chemotherapy. One way to verify consistency is to identify certain subgroups of subjects that might be expected to show a high use of chemotherapy. For example, one group that should have a very high rate of chemotherapy use is women aged 65 through 69 years with node-positive but estrogen receptor-negative tumors. We found that 70% of these women were identified as receiving chemotherapy by the Medicare data versus 5% of similarly aged women with node-negative and estrogen receptor-positive tumors (Table

Table 4. Multivariate Analysis for the Receipt of Chemotherapy Within 6 Months After Diagnosis in Women With Stages I, II, III and IV Breast Cancer in 1991 and 1992

Patient and Tumor Characteristics	No. of Cases (n = 10,604)	Odds Ratio* of Receiving Chemotherapy	95% Confidence Interval
Age			
65-69 years	2,893	1	—
70-74 years	2,901	0.60	0.51-0.70
75-79 years	2,280	0.33	0.27-0.40
≥ 80 years	2,530	0.11	0.08-0.14
Race			
White	9,754	1	—
Black	540	0.93	0.70-1.23
Other	310	0.66	0.43-1.02
Marital status			
Married	4,368	1	—
Unmarried	5,937	0.81	0.70-0.94
Unknown	299	0.68	0.42-1.10
Other cancer therapies			
No cancer-directed surgery	291	1	—
BCS only	1,446	0.95	0.63-1.45
BCS and RT	2,236	0.63	0.41-0.96
Mastectomy only	6,131	0.83	0.55-1.25
Mastectomy and RT	500	0.92	0.60-1.43
Tumor stage			
Stage I	5,824	1	—
Stage II	3,697	2.57	1.97-3.35
Stage III	654	4.83	3.38-6.89
Stage IV	429	4.04	2.77-5.89
Tumor size			
< 1.0 cm	1,976	1	—
1.0- < 2.0 cm	4,029	1.90	1.43-2.51
2.0- < 3.0 cm	2,278	1.69	1.24-2.32
3.0- < 4.0 cm	898	2.26	1.59-3.22
4.0+ cm	1,147	2.16	1.52-3.06
Unknown	296	2.98	1.99-4.50
Node and ER status			
Node-positive and ER-positive	1,741	1	—
Node-positive and ER-negative	335	3.60	2.77-4.68
Node-positive and ER unknown	418	1.26	0.96-1.65
Node-negative and ER-positive	3,879	0.26	0.20-0.34
Node-negative and ER-negative	689	1.97	1.49-2.60
Node-negative and ER unknown	1,319	0.38	0.27-0.53
Node not examined	2,223	0.88	0.68-1.15
Comorbidity index			
No claims	312	0.68	0.41-1.12
0	8,160	1	—
1	815	0.80	0.59-1.07
2	372	0.46	0.27-0.76
3+	945	0.94	0.77-1.16

*Adjusted for variables listed in the table.

3). Such internal consistencies support the validity of the information on chemotherapy in Medicare claims data.

It is important to understand the limitations of this study. The study findings were only applied to women ≥ 65 years of age who are not HMO members and who have both Medicare Part A and Part B coverage. Second, we used

cases with breast cancer diagnosed in the early 1990s. The information may not be the same as in the later years. Third, part of the information on chemotherapy may represent treatment of recurrent disease, not primary disease. For this reason, we restricted most of our analyses to chemotherapy received within 6 months of diagnosis. From the professional charge claims, we found that for some patients (12%), there are multiple line-items of service claims with payment on the same day associated with chemotherapy administration (data not shown). For others, there was one claim with a total amount of dollars for all services that were related to such a therapy. Some doctors may bill for the entire course of chemotherapy in one or two bills. However, in this study, the main interest was to see whether Medicare data could be used to identify women who had ever used chemotherapy within a certain time period after diagnosis, regardless of the number of courses or cycles of therapy. This would understandably be more accurate than identifying the true number of cycles of chemotherapy. Fourth, it is difficult to imagine this high percentage (12%) of women receiving just one treatment. Some may have experienced a toxicity that precluded further treatment. Also, the one claim may have represented more than one chemotherapy treatment. Fifth, data on comorbidity from this claims-based administrative database are less complete than data obtained from the medical chart reviews. Finally, a major concern is that the information on chemotherapy in Medicare claims data has not been validated against an external source such as medical chart review, as discussed above. Until such a validation study is performed, it is impossible to directly assess the accuracy and completeness of the information on chemotherapy in the Medicare claims.

Medicare claims data might be used to provide a population-based assessment of use of chemotherapy in the community. There are clear recommendations on the use of chemotherapy in women with breast cancer aged 65 through 69 years, but recommendations for women ≥ 70 years of age are less clear cut.¹⁻⁴ Thus greater variation among providers, facilities, and geographic areas in the use of chemotherapy in women ≥ 70 years of age compared with those who are 65 to 69 years of age might be expected. The claims data might be used to assess how well recommendations are being followed in the community for 65- to 69-year-old women. In addition, Medicare claims data on chemotherapy should allow for population-based effectiveness studies.

In conclusion, Medicare claims data seem to provide valuable information on chemotherapy for breast cancer, which is potentially important for describing the patterns of care in the population and for determining the effectiveness of chemotherapy in the community. However, external validation of the accuracy and completeness of these data is

an important step before any firm conclusion can be drawn with confidence.

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Increase of Chemotherapy Use in Older Women with Breast Cancer from 1991 to 1996

Running head: Trends in chemotherapy for breast cancer

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Précis

There was a significant increase of chemotherapy use in women aged ≥ 65 with breast cancer from 1991 to 1996. The increase was limited to younger women and those with advanced stage at diagnosis.

Abstract

Background. There is little population-based information available on the actual use of chemotherapy, and how closely this use mirrors consensus recommendations. We hypothesized that, given the relative stability of consensus conference recommendations on chemotherapy use during the period 1991-1996, the patterns of use in the community would more closely approximate consensus recommendation over time.

Methods. We studied women diagnosed with stage I-IV breast cancer at age 65 and older from 1991 through 1996, using the Surveillance, Epidemiology and End Results cancer registry cases linked with Medicare claims.

Results. Overall, women diagnosed in 1996 had a 30% higher chance of receiving chemotherapy than those in 1991, after controlling for changes in tumor size, stage and other factors. The use of chemotherapy was strongly influenced by age, with women 65-69 more than twice as likely to receive it as were women 70 and older. The increase over time in chemotherapy depended on both tumor stage and patient age. For stage I tumor there was no increase in chemotherapy for any age. For stage II the increase was limited to younger women, while for stage III and IV it was seen in women aged 70 and older.

Conclusions. There was a significant increase of chemotherapy use in women aged ≥ 65 with breast cancer over time from 1991 to 1996. The increase was limited to younger women and those with advanced stage at diagnosis. Thus, consensus recommendations and community practice seemed to mirror each other over time.

Key words: breast cancer, chemotherapy, women, elderly, Medicare, population-based.

Introduction

Chemotherapy has been demonstrated to be efficacious in women with breast cancer in numerous clinical trials over the past several decades.¹⁻³ However, the efficacy of chemotherapy and guidelines for its use vary by tumor stage and patient age.⁴⁻¹⁰ In the 1985 NIH consensus statement, combination chemotherapy was considered as the standard of care for premenopausal women and postmenopausal women aged less than 70 years with operable breast cancer with positive lymph nodes and for those with negative nodes with high-grade tumor histology or negative hormone receptors.⁴ This recommendation was essentially repeated in the 1990 and 2000 consensus conferences, with the additional statement that node negative tumors greater than 1 cm in size should be considered for adjuvant chemotherapy.^{5,8}

These consensus recommendations noted the lack of evidence of efficacy of adjuvant chemotherapy in women aged 70 years and older. Meta analysis have shown decreasing benefit from adjuvant chemotherapy with increasing age, though the numbers of women aged 70 and older enrolled in such trials has been small.¹⁻³ Accordingly, there are no clear recommendations for adjuvant chemotherapy in women aged 70 and older. For women with more advanced tumor (stages III and IV), systemic therapy (chemotherapy or hormonal therapy or both, depending on hormonal receptor levels) was recommended as primary therapy in both premenopausal and postmenopausal women.¹⁰

There is little information available on the actual use of chemotherapy in the community, and how closely this use mirrors consensus recommendations. The previous reports on the

prevalence of chemotherapy use have produced conflicting results.¹¹⁻²¹ A series of the national hospital-based surveys of breast cancer in the United States, organized by the American College of Surgeons,¹²⁻¹³ reported that 16.4% of women of all ages with local to distant breast cancer had used chemotherapy in 1976, and it increased to 22.7% in 1981. By 1991, 46.6% of women received chemotherapy or Tamoxifen (no specific data given on the use of chemotherapy only).¹² The prevalence of chemotherapy use in 17 community hospitals across the nation in 1982 in women aged 65-74 years was 55% for regional stage and 49% for distant stage.¹¹ In contrast, among women aged 65 or over with early stage breast cancer diagnosed in a large health maintenance organization, only 13% of them received chemotherapy in 1993-94.¹⁴

This study was conducted to assess temporal trends in the use of chemotherapy among women aged 65 and older diagnosed with breast cancer from 1991 to 1996, using the Surveillance, Epidemiology and End Results (SEER) cancer registry cases linked with Medicare claims. We hypothesized that, given the relative stability of consensus conference recommendations on chemotherapy use during this period, the patterns of use in the community would more closely approximate consensus recommendation over time. Because no clear recommendations exist for women aged 70 and older, we expected to see a closer approximation to consensus conference recommendations among women aged 65-69 than in older women.

Patients and Methods

Data sources

We used the merged Surveillance, Epidemiology and End Results (SEER)-Medicare database for women diagnosed with breast cancer in 1991 through 1996. The SEER program,

supported by the National Cancer Institute, includes population-based tumor registries in selected geographic areas:²² the metropolitan areas of San Francisco/Oakland, Detroit, Atlanta and Seattle; Los Angeles county; the San Jose-Monterey area; and the states of Connecticut, Iowa, New Mexico, Utah and Hawaii. These areas cover approximately 14% of the U.S. population. The registries ascertain all newly diagnosed (incident) breast cancer cases from multiple reporting sources such as hospitals, outpatient clinics, laboratories, private medical practitioners, nursing/convalescent homes/hospices, autopsy reports and death certificates.²³ Information includes tumor location, size, American Joint Committee on Cancer (AJCC) stage, axillary node status and estrogen receptor status; demographic characteristics such as age, gender, and race; and types of treatment provided within four months after the date of diagnosis.

The Medicare Program covers hospital, physician and other medical services for more than 97% of persons aged 65 years or older.^{24,25} The Medicare claims data used in the study included the following three files:²⁵ (1) Medicare Provider Analysis and Review file, which contains inpatient hospital claims; (2) the Hospital Outpatient Standard Analytic File, which contains the claims for outpatient facility services; and (3) the 100% Physician/Supplier file, which contains the claims for physician and other professional services. These data were available for all beneficiaries starting in 1991, and their Medicare claims are available through 1998.

Cases reported by the SEER registries from 1991 to 1996 have been matched against the Medicare master enrollment file. Of persons aged 65 and over appearing in the SEER records,

Medicare eligibility could be identified for 94% of these cases. The method of linking these data has been described elsewhere.²⁴

Study population

The study population consisted of all women aged 65 years or older who were diagnosed with breast cancer in 1991 through 1996 among the 11 SEER areas. For 1991 cases, the study covers only 9 SEER areas since there is no information released by SEER for cases diagnosed in 1991 in Los Angeles and San Jose-Monterey areas. Excluded were women who did not have full coverage of both Medicare Part A and Part B, or who were members of Health Maintenance Organizations (HMO), because claims from these organizations may not be complete. These left 35,060 patients with stages I to IV breast cancer for the analysis. Patient and tumor characteristics such as age, race, marital status, tumor stage, and geographic areas are available from the SEER data.

Chemotherapy

The detail of how we identified chemotherapy use through the Medicare claims was discussed elsewhere.²⁶ In brief, the following Medicare codes were used for defining chemotherapy: the ICD-9-CM procedure code of 9925 for a hospital inpatient or outpatient facility claim of chemotherapy (injection or infusion of cancer chemotherapeutic substance),²⁷ the Common Procedure Terminology codes of 96400-96549, J9000-J9999, and Q0083-Q0085 for a physician or outpatient claim of chemotherapy administration,^{28,29} revenue center codes of 0331 (chemotherapy injected), 0332 (chemotherapy oral) and 0335 (chemotherapy intravenous)

for an outpatient claim of chemotherapy,³⁰ and the ICD-9-CM V codes²⁷ of V58.1, V66.2, or V67.2 for follow-up examination or care after chemotherapy.

Surgery and radiation therapy

In SEER, cancer-directed surgery was defined as either mastectomy, which includes total/subcutaneous/radical/modified radical mastectomy, or breast-conserving surgery (BCS), which includes segmental mastectomy, lumpectomy, quadrantectomy, tylectomy, wedge resection, nipple resection, excisional biopsy, or partial mastectomy unspecified. The radiation therapy included beam radiation, radioactive implants, radioisotopes or other radiation as documented in SEER.²³

Comorbidity index

Comorbidity was ascertained from Medicare claims data through diagnoses or procedures made 1 year prior to the diagnosis of breast cancer. We used the comorbidity index created by Charlson et al³¹ and later validated by Romano and colleagues using the ICD-9-CM diagnosis and procedure codes.³² Both the Medicare inpatient and outpatient claims were searched for comorbid conditions, but not including breast cancer diagnosis codes (ICD-9-CM codes of 174x).

Analyses

Since SEER reported only the month and year of diagnosis of breast cancer, we arbitrarily defined the day of diagnosis in SEER as the 15th of the month. Chemotherapy from inpatient claims was defined as the date of admission. For outpatient and physician claims,

chemotherapy was defined as the earliest date of service. Chemotherapy was defined if there is at least one claim for chemotherapy within specified time periods after diagnosis (6 months or 24 months).

The odds ratios of receiving chemotherapy in women with various patient and tumor characteristics were generated from multivariate logistic regression analyses. These analyses adjusted for age, race, tumor stage, tumor size, node status and estrogen receptor status, and comorbidity indices, which are considered to likely affect the use of chemotherapy in women with breast cancer. All computer programming and analyses were completed using the SAS system.³³

Results

Table 1 presents the prevalence of chemotherapy use within 6 months of diagnosis in women with breast cancer diagnosed in 1991-1996, stratified by tumor stage. Overall, there was a small increase of chemotherapy use from 1991 to 1996. This pattern varied by tumor stage. There were significant increases in chemotherapy use in women with stages II-IV breast cancer, while in women with stage I cancer there was a non significant trend for decreased use over time.

Of 4134 (11.8%) patients who received chemotherapy within 6 months of diagnosis from 1991 through 1996, 3811 cases (92.3%) had Medicare J-codes, that specified what type of chemotherapy drugs were used. About 79% of women received fluorouracil, 62% for cyclophosphamide, 60% for methotrexate, and 30% received doxorubicin. The use of

doxorubicin and cyclophosphamide significantly increased over time, while the use of fluorouracil, methotrexate and mitoxantrone decreased slightly (Table 2). As expected, a newly approved agent, Taxol (Pactitaxel), was rarely used in the early 1990s, but its use increased in more recent years.

Table 3 presents the time trends in chemotherapy use according to lymph node and estrogen receptor status. As expected, women with node positive and estrogen receptor negative tumors had the highest rate of chemotherapy use (54.8% for all ages and 74.6% for those aged 65-69 for the period 1991 through 1996), and those with node negative and estrogen receptor positive tumors had the lowest rate (corresponding rate was 2.5% and 4.8%). There were significant increases in the use of chemotherapy for women with node positive tumors over time. For women with node negative and estrogen receptor positive, there was a small but significant decrease in chemotherapy use over this same period. For other node negative tumors, there was no change in use of chemotherapy.

As noted above, there were clear guidelines for use of adjuvant chemotherapy throughout the 1990's for women aged 65 through 69, while the recommendations for women aged 70 and older were less clear. When the data in Table 3 were stratified by age (65-69 vs 70 and older), there were non-significant trends for an increase in chemotherapy use for 65-69 years old women with node negative and estrogen receptor negative tumors ($P=0.077$), with a decrease in chemotherapy use for women aged 70 and older with those cancers ($P=0.058$).

Table 4 presents a multivariate analysis of odds of chemotherapy use by year of diagnosis (1991 to 1996) as well as other factors that might affect chemotherapy use. There was a marked decrease in chemotherapy with advancing age. As expected, large tumor size or higher stage was associated with greater use of chemotherapy, and the use of chemotherapy by node and estrogen receptor status was similar to that shown in Table 3. After adjusting for these other factors that influence chemotherapy use, the increase in chemotherapy over time became more apparent. For example, women with breast cancer diagnosed in 1996 had a 30% greater odds of receiving chemotherapy compared to those diagnosed in 1991.

Table 5 examines the interaction of age of the patient and tumor stage on the change in chemotherapy use from 1991 to 1996. The table presents the odds of receiving chemotherapy in 1995-96 compared to 1991-92, adjusted for other prognostic factors and stratified by age of the patient and tumor stage. In women with stage I breast cancer, there was no change in use of chemotherapy in 1995-96, compared to 1991-92 for all age groups. In women with stage II cancer, those aged 65-69 and 70-74 experienced greater use of chemotherapy over time, while those aged 75 or older did not. For women with stage III, there were significant overall increases in use of chemotherapy for all ages. A similar pattern was seen for stage IV cancer but the results were not all statistically significant.

Discussion

This study addressed recent trends in use of chemotherapy for women aged ≥ 65 diagnosed with breast cancer. Overall, there was a small increase of chemotherapy use over time from 1991 to 1996. However, after controlling for changes in tumor size, stage and other prognostic factors, women diagnosed in 1996 had a 30% higher chance of receiving chemotherapy than those in 1991. The increase in chemotherapy use was greater in the adjusted than unadjusted analyses because tumor prognostic factors at diagnosis, especially size, improved throughout the time period studied. The use of chemotherapy was strongly influenced by age, with women 65-69 more than twice as likely to receive it as were women 70 and older. The increase in chemotherapy over time depended on both the stage of the tumor and the age of the patient. For stage I tumor there was no increase in chemotherapy for any age. For stage II the increase was limited to younger women, while for stage III and IV it was seen in women aged 70 and older.

Overall and age-specific chemotherapy use did not increase in women with stage I (localized disease with negative lymph nodes) from 1991 to 1996. This is associated with the fact that the research evidence then and the 1990 NIH guidelines for treatment of breast cancer did not support the routine use of adjuvant chemotherapy in this group. For example, the 1990 NIH consensus statement stated that the majority of patients with node negative breast cancer (mainly stage I cancer) can be 'cured' by primary surgery and radiation. Women aged 65-69 years with stage II or higher breast cancer experienced significant increases in the use of chemotherapy over

time. The efficacy of chemotherapy has been well documented in postmenopausal women aged less than 70 years and it was clearly recommended.¹⁻¹⁰

In women over 70 years of age, however, there was no effect of chemotherapy on recurrence and mortality of early stage breast cancer, as reviewed by the Early Breast Cancer Trialists' Collaborative Group (EBCTCG) in 1988,¹ 1995² and 1998.³ The study by the EBCTCG concluded that "the apparent lack of any effect on recurrence and mortality for those aged 70 or older may chiefly reflect the adverse play of chance among the relatively small number of such patients that have been studied, but this remains a matter for research".³ This lack of evidence of efficacy resulted in no clear consensus recommendations on how to treat women in this age group. We observed a significant increase over time in chemotherapy use in women aged 70-74 with stage II cancer. There was also a significant increase of chemotherapy use in women aged 75 or older with more advanced tumor (stage III and stage IV).

One interesting piece of information is the use of specific chemotherapy agents over time from 1991 to 1996. This information can uniquely be identified through the analyses of the Medicare-J codes that specified what chemotherapy drug was used for over 92% of women with breast cancer. The use of doxorubicin and cyclophosphamide increased over time, but the use of fluorouracil, methotrexate and mitoxantrone decreased from 1991 to 1996. As expected, a newly approved agent, Taxol (Pactitaxel), was rarely used in the early 1990s, but its use increased in more recent years. This agent is often used at the later stage after other combination therapy such as doxorubicin and cyclophosphamide.³⁴ By examining the monthly claims for Taxol each year, the number of women using such a new drug increased gradually from 1991 through 1996,

without evidence of sudden jump of increase in any time point during these years (data not shown).

There are some limitations in this study. First, information on chemotherapy in Medicare claims data has not been validated against an external source such as medical chart review. However, we have demonstrated how Medicare claims codes can be used to identify women receiving chemotherapy, concluding that Medicare data provide valuable information on the use of chemotherapy in women known to have breast cancer in 1991-92.²⁶ Previous studies³⁵⁻³⁷ also demonstrated that Medicare claims data were of good validity in other aspects of breast cancer care (surgery and radiotherapy), which may serve as indirect support for the validity of information for chemotherapy use in Medicare. Second, the study findings may only be applied to women aged 65 and older who are not HMO members and have both Medicare Part A and Part B coverage in the year of diagnosis. We found that the number of subjects excluded slightly increased over time from 1991 to 1996 (data not shown). This may be chiefly because the number of subjects enrolled with HMO increased in more recent years, which could affect the results in this study. Third, chemotherapy used either for the recurrence of cancer or as part of the initial therapy cannot be clearly distinguished in Medicare. For this reason, we restricted our analyses to those with chemotherapy received within 6 months of diagnosis. By extending the time period of Medicare claims for chemotherapy from 6 months to 24 months after diagnosis, the patterns of use of chemotherapy were not affected (data not shown). Fourth, whether chemotherapy was used as primary therapy for more advanced disease or as adjuvant therapy for earlier stage cancer cannot be completely determined in the study. However, the analyses was stratified by tumor stage (Tables 1 and 5) and also by primary surgery and radiation therapy for

breast cancer (Table 4). These data were also adjusted in the multivariate analyses on the likelihood of chemotherapy use (Table 4). Fifth, analysis of temporal trends can be confounded by changes over time in accuracy and completeness of reporting. Thus, the increase in chemotherapy over time could be an artifact of more complete recording of chemotherapy billings in the Medicare data. In this regard, the fact that women with some tumor types showed no change or even decrease in chemotherapy use over time would argue against that possibility. Finally, information was presented for women diagnosed up to the year of 1996. The more recent trend after 1996 is unknown. Particularly, during the years 1997-1999, findings from the National Surgical Adjuvant Breast and Bowel Project Studies suggested that all women with breast cancer benefit from chemotherapy.³⁸ As a result, the use of chemotherapy in more recent years may be expected to increase more sharply.

In conclusion, there was a significant increase of chemotherapy use in women aged ≥ 65 with breast cancer over time from 1991 to 1996, after controlling for changes in tumor size, stage and other prognostic factors. The increase was limited to younger women and those with advanced stage at diagnosis. Thus, consensus recommendations and community practice seemed to mirror each other over time.

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Table 1. Prevalence of chemotherapy use in women aged 65 or older with breast cancer who had claims for chemotherapy made within 6 months of diagnosis, by tumor stage

AJCC tumor stage	Prevalence (%) of chemotherapy use, by year of diagnosis						P value for linear trend
	1991 * (n=4963)	1992 (n=6405)	1993 (n=6046)	1994 (n=5955)	1995 (n=5994)	1996 (n=5697)	
I (n=19141)	3.7	3.8	3.0	3.1	3.4	3.0	0.087
II (n=12350)	16.4	18.3	17.8	19.5	18.7	19.5	0.015
III (n=2206)	32.7	31.3	28.0	32.2	38.9	43.7	0.001
IV (n=1363)	27.8	31.3	35.8	33.3	37.2	40.9	0.003
Total (n=35060)	11.0	11.8	11.2	12.0	12.2	12.4	0.016

* Including cases for 9 SEER areas only in 1991, and in 1992-1996 cases were from 11 SEER areas (see Methods).

Table 2. Percentage of women with stages I-IV breast cancer 1991 to 1996 who received specific chemotherapy drugs that can be identified by Medicare claims made within 6 months of diagnosis

Name of chemotherapy drugs	Column Percentage of women who had claims for chemotherapy within 6 months of diagnosis (note: one patient could have claims for more than one drug agent)						P value for linear trend
	1991*	1992	1993	1994	1995	1996	
Doxorubicin	20.0	26.4	29.0	33.2	36.8	39.0	0.001
Cyclophosphamide	50.8	55.1	55.6	66.5	69.6	72.2	0.001
Fluorouracil	79.2	78.6	81.9	81.9	77.3	72.9	0.006
Methotrexate	59.9	61.0	65.7	58.2	55.6	58.2	0.029
Mitoxantrone	7.1	4.2	3.3	3.9	4.2	3.3	0.025
Paclitaxel (Taxol)	0	0	0.3	1.5	3.5	5.4	0.001
Other agents †	8.9	10.4	10.8	8.5	8.5	10.0	0.001
Agents unspecified	28.8	34.1	14.9	17.1	9.0	7.2	0.709
Any of above drugs	451 (100.0)	693 (100.0)	639 (100.0)	668 (100.0)	691 (100.0)	669 (100.0)	

* Including cases from 9 SEER areas only in 1991, and cases in 1992-1996 were from 11 SEER areas (see Methods).

† Other chemotherapy agents included drugs that were listed in Medicare under J-codes except for those in the table.

Table 3. Percentage of women receiving chemotherapy within 6 months after diagnosis in women aged 65 and older with stages I-IV breast cancer in 1991-96, by lymph node and estrogen receptor status

Lymph node and estrogen receptor (ER) status	n (%) of cases receiving chemotherapy, by year of diagnosis						P value for linear trend
	1991 * (n=4963)	1992 (n=6405)	1993 (n=6046)	1994 (n=5955)	1995 (n=5994)	1996 (n=5697)	
Node positive, and ER positive	20.3	24.5	23.0	24.1	24.3	27.0	0.008
Node positive, and ER negative	52.7	49.0	49.4	58.4	59.9	61.5	0.002
Node positive, and ER unknown	23.6	27.7	24.9	30.7	30.8	33.2	0.016
Node negative, and ER positive	3.0	3.3	2.8	2.6	2.0	2.0	0.003
Node negative, and ER negative	22.6	16.0	14.5	17.0	17.1	17.9	0.548
Node negative, and ER unknown	4.0	5.3	4.0	3.3	4.9	5.0	0.791
Node not examined	10.4	10.2	9.4	9.6	10.4	10.2	0.919
Total	547 (11.0)	756 (11.8)	679 (11.2)	715 (12.0)	729 (12.2)	708 (12.4)	0.016

* Including cases for 9 SEER areas only in 1991, and in 1992-1996 cases were from 11 SEER areas (see Methods).

Table 4. Multivariate analysis for the receipt of chemotherapy within 6 months of diagnosis in older women with stages I-IV breast cancer in 1991-96

Patient and tumor characteristics	Number of cases receiving chemotherapy (%)	Odds ratio* of receiving chemotherapy	95% confidence interval
Year of diagnosis			
1991	547 (11.0)	1	-
1992	756 (11.8)	1.11	0.97-1.27
1993	679 (11.2)	1.01	0.88-1.16
1994	715 (12.0)	1.15	1.00-1.32
1995	729 (12.2)	1.22	1.06-1.40
1996	708 (12.4)	1.30	1.13-1.49
Age (years)			
65-69	1819 (20.9)	1	-
70-74	1333 (13.9)	0.55	0.50-0.60
75-79	687 (8.7)	0.29	0.26-0.32
80+	295 (3.3)	0.08	0.07-0.09
Other cancer therapies †			
No cancer-directed surgery	301 (28.3)	1	-
BCS only	368 (7.1)	0.69	0.55-0.86
BCS and RT	668 (7.2)	0.52	0.41-0.65
Mastectomy only	2153 (12.0)	0.69	0.56-0.86
Mastectomy and RT	563 (34.7)	1.05	0.83-1.32
Tumor stage			
Stage I	638 (3.3)	1	-
Stage II	2272 (18.4)	2.86	2.47-3.30
Stage III	755 (34.2)	5.30	4.37-6.42
Stage IV	469 (34.4)	5.61	4.54-6.92
Tumor size (cm)			
<1.0	258 (3.9)	1	-
1.0-<2.0	999 (7.6)	1.74	1.49-2.03
2.0-<3.0	985 (13.4)	1.72	1.45-2.04
3.0-<4.0	561 (18.2)	1.89	1.56-2.29
4.0+	995 (25.9)	1.94	1.61-2.34
Unknown	336 (37.6)	2.52	2.00-3.17
Lymph Node and ER status ‡			
Node positive, and ER positive	1275 (23.8)	1	-
Node positive, and ER negative	712 (55.5)	4.25	3.69-4.89
Node positive, and ER unknown	402 (28.2)	1.30	1.13-1.50
Node negative, and ER positive	317 (2.6)	0.20	0.17-0.24
Node negative, and ER negative	403 (17.2)	1.46	1.25-1.70
Node negative, and ER unknown	177 (4.4)	0.37	0.31-0.45
Node not examined	848 (10.0)	0.73	0.64-0.84
Comorbidity index			
0	2891 (11.6)	1	-
1	428 (8.9)	0.82	0.73-0.93
2	180 (8.9)	0.82	0.69-0.98
3	66 (7.9)	0.68	0.51-0.90
4+	569 (22.8)	0.97	0.86-1.10

* Adjusted for factors listed in the table plus race (white, black, other), 9 SEER areas (San Francisco/Oakland was combined with Los Angeles county and the San Jose-Monterey area in California).

† Other breast cancer therapies include no cancer-directed surgery, breast-conserving surgery (BCS), radiation therapy (RT), and mastectomy.

‡ ER denotes estrogen receptor status.

Table 5. Effect of time period on receipt of chemotherapy in patients with breast cancer, stratified by tumor stage and patient age

Tumor stage and patient age (years)	Adjusted odds ratio (95% confidence interval) of receiving chemotherapy within 6 months of diagnosis in 1995-96 compared to 1991-92 †
Stage I	
65-69	0.99 (0.73-1.33)
70-74	0.96 (0.68-1.37)
≥ 75	0.80 (0.54-1.20)
All ages (≥ 65)	0.90 (0.74-1.09)
Stage II	
65-69	1.30 (1.07-1.58)*
70-74	1.32 (1.07-1.63)*
≥ 75	1.09 (0.86-1.38)
All ages (≥ 65)	1.15 (1.02-1.29)*
Stage III	
65-69	1.99 (1.22-3.24)*
70-74	1.68 (1.04-2.71)*
≥ 75	1.49 (1.02-2.18)*
All ages (≥ 65)	1.50 (1.19-1.88)*
Stage IV	
65-69	1.74 (0.98-3.09)
70-74	1.35 (0.75-2.43)
≥ 75	1.83 (1.10-3.05)*
All ages (≥ 65)	1.47 (1.10-1.96)*

* P<0.05 (Statistical significance of the odds ratios as compared to the reference group).

† Odds ratios were adjusted race (white, black, other), tumor size, other cancer-directed therapies, comorbidity index (0, 1, 2+), and 9 SEER areas (San Francisco/Oakland was combined with Los Angeles county and the San Jose-Monterey area in California).

Appendix 5 to 8. Copies of the abstracts published.

1. Du XL, Freeman JL, Nattinger AB, Goodwin JS. The effect of axillary node dissection on survival in women with early stage breast cancer. American Journal of Epidemiology. 2000;151(suppl):S64.
2. Du XL, Goodwin JS. Patterns of use of chemotherapy for breast cancer in older women: findings from Medicare claims data. Gerontologist. 2000;40(Special Issue I):344-345.
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THE EFFECT OF AXILLARY NODE DISSECTION ON SURVIVAL IN WOMEN WITH EARLY STAGE BREAST CANCER. XL Du,* JL Freeman, AB Nattinger, and JS Goodwin (University of Texas Medical Branch, Galveston, TX 77555)

Increasing numbers of older women with early stage breast cancer are receiving breast-conserving surgery (BCS) without axillary dissection. While such an approach appears efficacious in randomized controlled trials, there is concern that it contributes to higher breast cancer mortality in the community. We studied 26,290 women aged ≥ 25 in 1983-93 from the Surveillance, Epidemiology and End Results (SEER) Program and 5,328 women aged ≥ 65 in 1991-93 from SEER-Medicare linked data, who had an early stage breast cancer and received BCS. Overall, 27% of women aged ≥ 25 receiving BCS did not receive axillary dissection, most of whom (74%) were age ≥ 65 . Women receiving BCS with axillary dissection had lower 7-year breast cancer-specific mortality than did those without axillary dissection (Cox proportional hazard ratio=0.53, 95% confidence interval: 0.44-0.63). Women not receiving axillary dissection actually had a lower chance of receiving radiation or chemotherapy than those receiving axillary dissection. Of women receiving BCS without axillary dissection, 62% also did not receive radiation therapy and 98% did not receive chemotherapy. We found an interaction between receipt of axillary dissection and radiotherapy on survival of older women after BCS. Women who received either axillary dissection or radiotherapy experienced similar survivals to those who received both axillary dissection and radiation, while women who received neither treatment experienced poorer survival (hazard ratio=1.76, 1.23-2.52), after controlling for demographics, tumor size and comorbidity. The findings suggested that the combination of no axillary dissection plus no radiation after BCS is associated with an unacceptably high level of deaths from breast cancer. The lack of improvement in the past 2 decades in survival of older women with breast cancer may be explained in part by the increasing use of treatments that do not address potential tumor in axillary nodes.

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PROGESTIN USE WITH ESTROGEN IN RELATION TO ENDOMETRIAL CANCER RISK. P.A. Newcomb* and A. Trentham-Dietz (Fred Hutchinson Cancer Research Center, Seattle, WA 98104)

Both cyclic and continuous progestin use is associated with a much lower risk of endometrial cancer risk than estrogen alone; however, results are conflicting as to the optimum progestin regimen. Data from a population-based case-control study were analyzed that included 591 cases (87% of eligible) of endometrial cancer aged 40-79 years, newly diagnosed in 1991-94 and reported to Wisconsin's statewide cancer reporting system. Similarly aged population controls (N = 2045, 85% of eligible) were randomly selected from lists of licensed drivers and Medicare beneficiaries. In a structured telephone interview each episode and type of postmenopausal hormone use was ascertained as well as other endometrial cancer risk factor information. The relative risk (RR) for any use of estrogen use alone was 3.19 (95% CI 2.40-4.24), or 14% per year of use (95% CI 1.10-1.17). The RR for any use of estrogen+progestin was 1.79 (95% CI 1.22-2.61), or 7% per year of use (95% CI 1.01-1.13). The RR for use of progestins for less than 10 days per month was 2.58 (95% CI 1.05-6.37); for 10-24 days per month it was 1.17 (95% CI 0.63-2.18); and for continuous use it was 2.42 (95% CI 1.36-4.31). These data suggest that endometrial cancer risk does not simply decrease with increasing numbers of days per month of progestin use and the optimum duration and dose is not currently in use.

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ESTROGEN-PROGESTIN USE IN RELATION TO RISK OF LOBULAR AND DUCTAL BREAST CANCER. P.A. Newcomb,* L. Titus-Ernstoff, K.M. Egan, A. Trentham-Dietz, J.A. Baron, W.C. Willett, and M.J. Stampfer (Fred Hutchinson Cancer Research Center, Seattle, WA 98104)

Recent evidence suggests the addition of progestins to postmenopausal estrogens adversely affects breast cancer risk. Postmenopausal hormone use was assessed in 5157 incident invasive breast cancer cases (83% of eligibles) aged 50-79 years identified from statewide tumor registries in Massachusetts, New Hampshire, and Wisconsin, and 5459 controls (78% of eligibles) randomly selected from population lists. In a structured telephone interview each episode and type of postmenopausal hormone use was ascertained as well as other risk factor information. The relative risk (RR) of breast cancer associated with ever use of estrogen only (RR 1.20, 95% CI 1.07-1.35) was slightly lower than for estrogen-progestin use (1.44, 95% CI 1.19-1.75, p for difference 0.10). Risk increased with longer duration of hormone use, about 2% per year (95% CI 1.01-1.03) for estrogen, but for estrogen-progestin use the increase was 8% per year (95% CI 1.00-1.17). Although risk declined with increasing time since last estrogen use, no attenuation in risk was evident following cessation of estrogen-progestin use. Lobular histology was more strongly associated with estrogen-progestin use (RR 2.11, 95% CI 1.30-3.42) than ductal lesions (RR 1.42, 95% CI 1.13-1.78), whereas use of estrogen alone was similarly associated with lobular (RR 1.20, 95% CI 0.89-1.62) and ductal histology (RR 1.21, 95% CI 1.05-1.39). The elevated risk for hormone use was similar for localized and advanced disease. These data suggest that the increased risk associated with estrogen and progestin use appears to be greater than for estrogen alone, and may be sustained after cessation. Intriguingly, the increase in risk appeared most strongly associated with lobular breast histology.

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HORMONE REPLACEMENT THERAPY IN RELATION TO RISK OF LOBULAR AND DUCTAL BREAST CANCER IN MIDDLE-AGED WOMEN. C. Li,* N. Weiss, J. Stanford, and J. Daling (Fred Hutchinson Cancer Research Center, Seattle, WA 98109-1024)

Background: In most studies, long-term, recent use of hormone replacement therapy has been associated with an increased risk of breast cancer. However, little attention has been paid to the possibility that the magnitude of this association varies according to the histologic type of breast cancer. Methods: Interviews were conducted with 537 female residents of King County, Washington who were 50 to 64 years of age and who had been diagnosed with primary invasive or in situ breast cancer between January 1, 1988 and June 30, 1990. Interviews with 492 randomly selected King County women without a history of breast cancer served as a basis of comparison. Separate analyses were done for women with lobular and ductal tumors, as determined from pathology reports available to the population-based tumor registry that serves King County. Results: Compared with non-users of menopausal hormones, those who were currently using combined estrogen-progestin therapy and had done so for at least six months had an elevated risk of lobular breast cancer (odds ratio [OR] = 2.6; 95% confidence interval [CI], 1.1 to 5.8), but no change in their risk of ductal breast cancer (OR = 0.7; 95% CI, 0.5 to 1.1). The odds ratio associated with current use of unopposed estrogens for at least six months was 1.5 (95% CI, 0.5 to 3.9) for lobular tumors and 0.7 (95% CI, 0.4 to 1.1) for ductal tumors. Conclusions: The results of this study suggest that combined estrogen-progestin hormone replacement therapy may increase the risk of lobular breast cancer in middle-aged women.

Cancer pts who showed "inconsistent" decision making about nonaggressive care tended to be male (69% vs. 56), have higher incomes, and to perceive a better chance for 6-month survival ($p<.001$). Physicians of these pts also were more optimistic about their survival ($p<.001$). Whereas 74% of "inconsistent" decision makers were pts themselves (vs. surrogate respondents), only 51% of consistent decision makers were pts. The majority of both types of decision makers did not survive six months after study entry. Findings indicate that a subgroup of late stage cancer patients who favor nonaggressive care still prefer specific aggressive treatments. This raises questions about language used, pts' understanding, and the need for adequate communication before implementation of decisions in order to respect patient autonomy.

Predictors of Discharge Placement among Hospitalized Frail Elders

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Functional decline and chronic conditions complicate discharge planning for frail elders. In a study of exercise, 40 men and 117 women ($M=78$ years) were discharged to either home or skilled care. Those with a history of rehospitalization ($\chi^2=5.51$; $p<.01$), physical therapy after discharge (PT), and poorer balance and gait were more likely to be placed into skilled care. The predictors of discharge placement examined were number of medications, physical therapy after discharge (PT), length of stay less than 7 days (LOS), primary diagnosis, rehospitalization history, and comorbidity (Charlson Index); gait and balance (Tinetti gait and balance scale), and muscle strength of the knee (dynamometry), that was measured during hospitalization, were examined to determine if these factors would predict placement. Significant predictors ($\chi^2=33.29$; $p<.001$) were: PT (Exp (β) 10.97; $p<.05$), and balance (Exp (β) 0.75; $p<.05$). Patients who receive PT after hospital discharge and those with poor balance are at risk for placement into skilled care. Interventions targeted to improve balance such as muscle strengthening exercise may reduce this risk. (R01NR04012)

CORRELATES OF COLORECTAL CANCER SCREENING AMONG MEDICARE BENEFICIARIES

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Medicare began coverage of fecal occult blood testing (FOBT), a clinical procedure to screen for colorectal cancer, on January 1, 1998. The purpose of this study was to examine FOBT use rates among Medicare beneficiaries in Kansas, to determine if FOBT use was related to demographic or geographic variables, and to assess FOBT use rate changes across a two-year span. Statewide FOBT rates for 1998-1999 were determined by retrospective Medicare Part B claims analysis for all Kansas beneficiaries between the ages of 65 and 99 (mean age=75). Of the 358,816 beneficiaries in 1998 and the 360,506 beneficiaries in 1999, 4.70% had received a FOBT in 1998 and 5.15% in 1999. After adjusting for covariates, multivariate logistic regression revealed that having a FOBT was associated with being between the ages of 65-79 (compared to 50-64 and 80-99), being Caucasian, and living in a densely populated county. The general population and almost all subsets (age group, gender, race, and population

density) had higher FOBT rates in 1999 compared to 1998. The number of people who were screened steadily increased in 1998 (from 942 in January to 1564 in December, with a mean increase rate of 4.32% per month). Testing was stable in 1999 ($M=1,548$ per month). Based on a cohort of those who were eligible beneficiaries in both 1998 and 1999 ($N=343,152$), only 1.5% had an annual test and 69% of those who had a FOBT in 1998 were not screened again in 1999. Although screening for colorectal cancer with FOBT has increased from 1998 to 1999, the overall rates remain extremely low. This may be indicative of the small monetary amount (\$3.50) that providers are reimbursed to perform FOBT.

POTENTIALLY INAPPROPRIATE PRESCRIPTIONS AMONG THE COMMUNITY-DWELLING ELDERLY Chunliu Zhan, J. Sangl, G. Meyer, A. Bierman, S. Wickizer, J. Oh, B. Friedman

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This study examines the prevalence of potentially inappropriate drug prescriptions among the U.S. community-dwelling elderly in 1996 using explicit criteria developed by experts in geriatrics and pharmacology. These criteria identify medications that should be generally avoided because they pose unnecessarily high risks for the elderly. Data are from the 1996 Medical Expenditure Panel Survey. In 1996, 21.8% of community-dwelling elderly used at least one of the 38 drugs identified as inappropriate, with 8.8% using at least one of 17 considered to have severe adverse effects. One-fourth took two or more inappropriate drugs. Major classes of inappropriate drugs are analgesics (21.5%), antihistamine (17.4%), antidepressants (14.7%) and sedatives (8.5%). Males, individuals with poorer health status, and, most significantly, those using a larger number of medications are more likely to have inappropriate drug use. These results are comparable to a prior study using 1987 NMES data where 23.5% of elderly used at least one of 20 drugs identified as inappropriate based on earlier explicit criteria. This study highlights that the high prevalence of inappropriate drug prescribing for community-dwelling elderly continues even as guidelines exist. Recommendations are made for the development of educational policies and system improvements to reduce the prevalence of inappropriate medications among elderly persons residing in the community.

Patterns of use of chemotherapy for breast cancer in older women: findings from Medicare claims data

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Objectives: There is little information available on the use of chemotherapy in women with breast cancer. This study describes the use of chemotherapy through analysis of Medicare claims, and determines the correlates of chemotherapy use. **Methods:** We used the merged Surveillance, Epidemiology and End Results-Medicare database and identified women diagnosed with breast cancer at age ≥ 65 years in 1991-92. Chemotherapy was ascertained from Medicare claims through procedure codes for chemotherapy made <24 months after the diagnosis. **Results:** In women with stages I to IV, the percentage receiving chemotherapy <24 months of diagnosis was 4.9%, 19.3%, 34.2% and 34.3%, respectively. Most women receiving chemotherapy had 2 to 12 claims; the median number was 9.

Use of chemotherapy decreased significantly with age across all tumor stages; e.g. in women with stage III cancer, from 49% in those aged 65-69 to 10% in those aged ≥ 80 years. In a multivariate analysis, there was little variation by ethnicity. Chemotherapy use was highest (70%) in women aged 65-69 with node positive and estrogen receptor negative tumors, and low (4%) in those with node negative and estrogen receptor positive tumors. As compared to those without comorbid diseases, patients with comorbidity score of 2 had significantly lower use of chemotherapy. **Conclusions:** Medicare claims data appear to provide valuable information on the use of chemotherapy for breast cancer in older women. However, external validation of the accuracy and completeness of these data is required before any firm conclusion can be drawn.

COST OF NURSING-BASED CONSTIPATION CARE IN NURSING HOMES.

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Constipation is a common disorder among nursing home residents and affects at least half of all residents. Despite this, the actual costs for constipation care have not been determined in the nursing home setting. We used an observational time and motion design to obtain cost estimates of the burden of constipation care. Residents with chronic constipation from 2 nursing homes were identified and nursing staff performance of all constipation-related tasks were timed (12 hours/resident, N=59, median age = 88 yrs). Tasks observed were constipation evaluation and enema, suppository, dietary supplement, and oral medication administration. Task frequency, medication, and supply data were obtained through 60-day retrospective medical record review. Total annual costs per resident with constipation were calculated using median US wage rate data multiplied by staff time per task, with medication and supply costs added. Total costs were \$2253 per resident per year. Administration of oral medications (\$1950) and dietary supplements (\$225) were the most costly tasks. Each oral medication administration required 4.6 minutes on average and occurred 2.5 times per day per resident. Enema administration required 4.5 minutes and dietary supplement administration required 3.6 minutes per occurrence. Despite the prevalence of constipation in nursing homes, this study is the first empirical examination of the nursing home cost of the disorder. Results indicate that nursing staff and supply costs for constipation care is substantial due largely to multiple oral medication administrations per patient per day. This research was supported by Janssen Research Foundation.

MEDICATION USE AND HEALTH-RELATED QUALITY OF LIFE (HRQOL) AMONG ELDERLY

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With the increase in longevity many elderly are experiencing, it is important to address factors related to health-related quality of life. Medication use is a significant component of the lives of elderly as they deal with chronic health conditions in these extended years. The objective of this study was to examine the relationship between current prescription drug use and responses to a mail survey version of the CDC's Behavioral Risk Factor Surveillance Survey (BRFSS) HRQOL Module. The sample was comprised of 84,065 participants in Pennsylvania's Pharmaceutical Contract for the Elderly (PACE) (mean age=78.7). Controlling for demographics and other prescription medication use, any prescription drug use in each of 10 drug classes predicted self-rated health, number of "not good"

physical and mental health days, and number of activity limitation days ($p<.001$). Results of multivariate logistic regression analyses controlling for other medication use indicated that any drug use in each drug category, with the exception of cardiovascular, predicted the need for routine or personal care (O.R.=1.1-2.0, $p<.001$). CNS drugs were the most influential. Significant associations were found between number of medications used and the number of "pain" days, "sad, blue or depressed" days, "worried, tense or anxious" days, and days with not good sleep ($p<.001$). Results will also be presented according to gender differences. These findings indicate the importance of current prescription drug use as a factor in the quality of life of older persons.

Do African American and White Veterans with Chronic Knee and Hip Pain Differ with Respect to Their Knowledge about Joint Replacement Surgery and Its Risks and Benefits?

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Previous studies have reported ethnic differences in utilization of joint replacement, with lower rates among African-Americans (AA) as compared to Whites, but the reasons for these differences remain unknown. We examined ethnic differences in 563 older male AA (44%) and White (56%) VA patients with chronic knee and/or hip pain regarding their awareness of joint replacement and its risks and benefits.

AAs were less likely than whites to have heard of JR (adjusted OR = 0.61, 95% CI 0.36 - 1.02 to have known someone who had this surgery (adjusted OR = 0.32, 95% CI 0.21 - 0.49), to have a good understanding of hip/knee replacement surgery (adjusted OR = 0.60, 95% CI 0.41 - 0.88). AAs were more likely to believe that there will be moderate to severe pain post-JR (adjusted OR = 2.32, 95% CI 1.56 - 3.44) and they were also more likely to believe moderate to severe difficulty in walking post-JR (adjusted OR = 2.52, 95% CI 1.69 - 3.77). Odds ratios were adjusted for age, educational level, income, disease severity, health status and other important clinical and psychosocial covariates.

Overall, AAs, as compared to whites, were less likely to be aware of JR as an option for their arthritis as well as have a good understanding of its potential benefits. While AAs are less likely to utilized JR as an option for arthritis, these results suggest that lack of information about the benefits of JR may play a role in the disparities in utilization.

SHIFTING FROM SPECIFIC TREATMENT PREFERENCES TO GOALS OF CARE. TR Fried, EH

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Traditional methods of eliciting preferences for clinical treatment decisions have focused on the therapies themselves. This may not be congruent with patients' formulation of these decisions. The purpose of this study was to create a patient-centered instrument for eliciting treatment preferences.

Focus groups and individual interviews were conducted with 20 patients age ≥ 60 years seriously ill with CHF, COPD, or cancer focusing on treatment decision-making. The new instruments were based on themes found in qualitative analysis. Test-retest reliability was conducted with 20 patients, and internal reliability and validity with 72 patients.

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FASTING PLASMA LIPIDS AND BREAST CANCER INCIDENCE. PJ Mink*, E Shahar, WD Rosamond, AJ Alberg and AR Folsom (University of Minnesota, Minneapolis, MN 55454)

Plasma lipids and lipoproteins have been considered as risk factors or markers of breast cancer, possibly mediating a putative effect of dietary fat intake. High density lipoprotein cholesterol (HDL-C) levels have been associated with several breast cancer risk factors. We followed 7,828 women, age 45-64, in the Atherosclerosis Risk in Communities (ARIC) Ancillary Cancer Study. At baseline, a fasting blood sample was drawn and total cholesterol (TOT-C), low density lipoprotein (LDL-C), HDL-C, and triglyceride (TG) levels ascertained. Information on breast cancer risk factors was collected by questionnaires. Over an average follow-up of 7.1 years, 182 incident cases were identified. The multivariate-adjusted relative risk (RR) for women in the highest versus lowest quintile of TOT-C was 0.66 (95% Confidence Interval (CI): 0.39-1.11), but the test for trend was not significant ($p=0.24$). We observed an inverse association of LDL-C with breast cancer incidence: RRs for increasing quintiles were 1.0 (ref), 0.91, 0.70, 0.72, 0.55, respectively ($p\text{-trend}=0.08$). These associations were not attenuated when analyses were repeated after excluding cases identified within three years of baseline. HDL-C and TG levels were not associated with breast cancer incidence. Although HDL-C levels were associated positively with education, alcohol, hormone replacement therapy, and later age at first birth, our findings do not support hypotheses that HDL-C is associated with breast cancer risk. The inverse associations of breast cancer with TOT-C and LDL-C were unexpected. Longer follow-up may determine whether lower TOT-C and LDL-C levels are a cause or consequence of breast cancer.

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INSULIN-LIKE GROWTH FACTORS AND BREAST CANCER RISK IN CHINESE WOMEN. H Yu*, F Jin, B Li, XO Shu, Q Dia, H Berkel and W Zheng (Louisiana State University Health Sciences Center, Shreveport, LA 71130-3932)

Insulin-like growth factor (IGF)-I has mitogenic and anti-apoptotic effects on breast cancer cells. High circulating IGF-I are associated with increased risk of breast cancer. So far, all epidemiologic studies reported on IGF and breast cancer have been conducted mainly in Caucasian populations; little is known about the role of IGF-I in Asian women. Since these populations have different dietary habits, and serum IGF-I is influenced by energy and protein intake, we conducted a population-based case-control study to assess IGF-I and breast cancer risk in Chinese women. The study included 300 incident breast cancer patients and 300 age-matched controls. Plasma levels of IGF-I, IGF-II and IGFBP-3 were measured using commercial ELISA kits (DSL, Texas). Conditional logistic regression analysis was performed to examine the association of IGF with breast cancer risk. The study showed that breast cancer patients had higher levels of IGF-I, IGF-II, and IGFBP-3 in plasma than the controls and that high levels of IGF-I and IGFBP-3 were associated with increased risk of breast cancer. When comparing women with the highest tertile of IGF-I or IGFBP-3 to those with the lowest tertile, the odds ratios for breast cancer were 2.01 (95% CI: 1.26-3.19) for IGF-I and 3.01 (95% CI: 1.81-4.99) for IGFBP-3. These associations were dose-dependent and were more evident in premenopausal women. No association was found for IGF-II. The study confirms that high IGF-I is associated with increased risk of breast cancer.

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INCREASE OF CHEMOTHERAPY USE IN OLDER WOMEN WITH BREAST CANCER FROM 1991 TO 1996. X Du* and J Goodwin (University of Texas, Galveston, TX 77555)

There is little population-based information available on the use of chemotherapy, and how closely this use mirrors consensus recommendations. We hypothesized that, given the relative stability of consensus conference recommendations on chemotherapy use during the period from 1991 to 1996, the patterns of use in the community would more closely approximate consensus recommendation over time. We studied women diagnosed with stage I-IV breast cancer at aged 65 and older from 1991 through 1996, using the Surveillance, Epidemiology and End Results cancer registry cases linked with Medicare claims. Overall, women diagnosed in 1996 had a 31% higher chance of receiving chemotherapy than cases in 1991, after controlling for changes in tumor size, stage and other factors. Chemotherapy use was strongly influenced by age, with women 65-69 more than twice as likely to receive it as were women 70 and older. The increase in chemotherapy over time depended on both tumor stage and patient age. For stage I tumor there was no increase in chemotherapy for any age. For stage II the increase was limited to younger women, while for stage III and IV it was seen in women aged 70 and older. Women with node positive and estrogen receptor negative tumors had the highest rate of chemotherapy use (54.8% for all ages and 74.6% for those aged 65-69 for the period 1991 through 1996), while those with negative node and estrogen receptor tumors had the lowest rate (corresponding rates 2.5% and 4.8%). In conclusion, there was a significant increase of chemotherapy use in women with breast cancer over time from 1991 to 1996. The increase was limited to younger women and those with advanced stage at diagnosis.

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IS THERE A DIFFERENCE IN SURVIVAL OF BREAST CANCER AMONG FIRST AND SECOND GENERATION CHINESE AND WHITE WOMEN IN THE UNITED STATES? . F Shi*, N Birkett, Y Chen and E Grunfeld (University of Ottawa, Ottawa, ON K1H 8M5 Canada)

We compared the survival rates of breast cancer among first and second generation Chinese and White women in the United States, using the data from the Surveillance Epidemiology, and End Results (SEER) Program. Of a total of 115,632 female patients diagnosed with breast cancer between 1973 and 1992, we identified 543 first generation Chinese, 618 second generation Chinese and 114,471 Whites based on the information on ethnicity and birthplace. Second generation Chinese women had a better survival rate of breast cancer as compared to first generation Chinese and White women before adjustment for other variables. However, 62.2% of second generation Chinese women with breast cancer were from the Hawaii registry, which had a better survival than other registries, as compared to 11.0% of first generation Chinese and 1.5% of Whites from the Hawaii registry. In addition, second generation Chinese women had a higher percentage of localized breast cancer when compared with other two groups (60% vs 55% and 51%). After adjustment for age, stage, surgical treatment, and cancer registries using a Cox regression model, the difference in survival among three groups was no longer significant. Stage of disease at diagnosis and having surgical treatment were significantly related to the survival of breast cancer, which were independent of other variables included in the model. Our analysis suggests that the survival of breast cancer may be similar among the first and second generation Chinese and White women living in the United States.

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PATIENT ASSESSMENTS OF THE STIGMA ASSOCIATED WITH THE USE OF COMMUNITY-BASED DIRECTLY OBSERVED THERAPY (DOTS): A Katamba*, D Neuhauser, K Smyth, E Katabira, C Rwabukwali and C Whalen (Case Western Reserve University, Cleveland, OH 44106)

BACKGROUND: Tuberculosis (TB) remains a major cause of morbidity and mortality. To improve compliance with anti-TB therapy, the World Health Organization introduced the DOTS strategy. DOTS in the rural communities may not be universally acceptable, however, because of stigma resulting from the linkage of TB and HIV/AIDS. **OBJECTIVE:** To assess whether TB patients on DOTS are concerned about its potential stigmatizing effects. **DESIGN:** Cross-sectional study in communities in Kiboga and Mubende districts, Uganda. **METHODS:** A questionnaire, which recorded attitudes towards DOTS, TB and HIV infection, and socio-demographic and psychological variables, was administered to 105 TB patients on DOTS and 202 patients on self-administered therapy. **RESULTS:** Patients on DOTS were more likely to be males than other patients (74%vs.65%, respectively) but were of the same mean age (35years). The documented prevalence of HIV in the DOTS and non-DOTS patients was 29% and 34% respectively. Patients on DOTS were more likely to believe that neighbors knew they had TB compared to patients not on DOTS, (91%vs.61%, $p<0.001$). However, DOTS patients were no more likely than non-DOTS patients to believe that neighbors thought they had HIV because of TB (41%vs.36% $p=0.43$) or to believe that neighbors would spend less time with them since they got TB (26vs.17; $p=0.41$). **Conclusion:** The study demonstrated that the TB patients did not find the DOTS strategy stigmatizing. Therefore, wide implementation of the DOTS strategy by TB control programs should be feasible in the rural communities.

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PATTERNS OF MORBIDITY IN CHILDHOOD DETERMINED USING ADMINISTRATIVE HEALTH CARE DATA. DW Spady*, LW Svenson, DP Schopflocher and RS Sauve (University of Alberta, Edmonton, AB T6G 2R7 Canada)

Fee-for-service [FFS] health care data maintained by Alberta Health & Wellness were used to describe patterns of morbidity in Alberta children aged 0 - 17 years during the period 04/01/95 to 03/01/96. The data contain ICD9 codes describing the diagnosis provided by physicians when submitting a fee. Data were grouped into 17 categories based on ICD9 chapter headings. For each chapter, diagnoses were grouped into sub-categories describing diseases with common symptoms. Morbidity rates, stratified by age, sex, and subsidy group (proxy for socio-economic status) were calculated for each category and sub-category using the entire registered population of children as the denominator. Among 749924 children, there were 3,461,623 FFS events with diagnoses attributed. Services were provided in a physician's office (82.5%), an emergency room (ER) (9.2%), or in a non-ER hospital location (8.3%). Contact with the medical system varied from 97.8% at age 0 to 77.8% by age 12. Respiratory disease and disorders of the CNS and sense organs accounted for over 50% of all visits from age 1 to 8. Injury and poisoning accounted for up to 15% of visits after age 9. Gender variation was obvious for mental disorders, genitourinary disorders, and injury and poisoning. Patterns varied with premium subsidy status with those on welfare generally having higher rates of utilization. These results describe why children visit doctors and indirectly describe patterns of childhood illness. This overview of illness patterns provides a unique perspective of the health of children living under a wide variety of socioeconomic and geographic conditions.

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PATIENT FACTORS ASSOCIATED WITH CONTINUITY IN PRIMARY CARE: A CANADIAN STUDY. JE Arnold Gilbert* and PC Coyte (University of Toronto, Department of Health Administration, Toronto, ON M5M 3T2 Canada)

The elements of knowledge, trust and values are central to the discussion of whether or not a patient will choose to maintain a continuous relationship with his or her physician. The objective of this study was to identify patient characteristics associated with continuity of care. In this study, the definition of continuity was the dispersion of a patient's primary care visits among all family physicians seen over a two-year period of time. This study looked at a sample of respondents to the 1994-95 National Population Health Survey (NPHS), a Canadian population-based survey. These data were linked to administrative data from the Ontario Health Insurance Plan (OHIP) for information about primary care visits. Using the Continuity of Care (COC) score, multivariate modeling identified usual daily activity, income and an age-health interaction as significant in predicting continuity of care. The 12-24 age group had the smallest slope with regard to continuity (beta=-0.08, $p<0.005$) and all age groups over 45 had positive and statistically significant slopes. Individuals who were retired had a significantly positive slope compared to those working at home (beta=0.04, $p<0.05$). The group attending school had significantly lower continuity scores (beta=-0.08, $p<0.05$). The middle income group had a positive and borderline statistically significant slope, (beta=0.03, $p<0.05$). In total, 10.4% of the total variance in continuity of care scores could be explained by these factors ($R^2=0.104$). The role of patient values and the relative importance of process and outcome in primary care are discussed in light of these findings.

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USING MEDICARE DATA TO EXAMINE THE PATTERNS OF CHEMOTHERAPY USE FOR OLDER WOMEN WITH BREAST CANCER . X Du* and J Goodwin (University of Texas, Galveston, TX 77555)

Population-based information on the actual use of chemotherapy in women with breast cancer is scarce. The national Surveillance, Epidemiology and End Results (SEER) tumor registries do not report data on chemotherapy because of concerns about their completeness. Medicare program covers hospital/physician services for >97% of persons aged ≥ 65 . If Medicare claims data are valid, it could lead a new way to study variations in oncology care and to allow for effectiveness studies of chemotherapy in the community that fall outside the randomized settings. However, no study has yet examined the utility of Medicare claims for chemotherapy. This study used the SEER-Medicare linked data to describe use of chemotherapy through analysis of Medicare claims, and to determine internal validity and correlates in breast cancer women aged ≥ 65 in 1991-92. In women with stage I to IV, percentage receiving chemotherapy within 6 months of diagnosis was 3.6%, 16.3%, 29.9% and 26.3%, respectively. It decreased significantly with age across all tumor stages; e.g. in women with stage III, from 49% in those aged 65-69 to 10% in those aged 80+. In a multivariate analysis, odds ratio of receiving chemotherapy was 0.60 (95% CI: 0.51-0.70) for age 70-74, 0.33 (0.27-0.40) for 75-79, and 0.11 (0.08-0.14) for 80+, compared to 65-69. Chemotherapy use was highest (70%) in women aged 65-69 with node positive and estrogen receptor negative tumors, and lowest (4%) in those with node negative and estrogen receptor positive. In conclusion, Medicare data appear to provide valuable information on use of chemotherapy for breast cancer, but external validation of the data is still required.

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Survival of Women After Breast Conserving Surgery for Early Stage Breast Cancer

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Abbreviations:

AJCC stages: American Joint Committee on Cancer stages

BCS: Breast Conserving Surgery

SEER: Surveillance, Epidemiology and End Results

Abstract (245 words)

Increasing numbers of older women with breast cancer are receiving breast-conserving surgery (BCS). However, substantial numbers of them are not receiving either axillary dissection or adjuvant irradiation. To determine whether failure to perform axillary dissection or irradiation is associated with decreased survival in women with early-stage breast cancer, we studied 26,290 women aged ≥ 25 in 1988-1993 from the Surveillance, Epidemiology and End Results (SEER) data and 5,328 women aged ≥ 65 in 1991-1993 from SEER-Medicare linked data, who had early-stage breast cancer and received BCS. Twenty seven percent of women aged ≥ 25 receiving BCS did not receive axillary dissection, most of whom (74%) were age ≥ 65 . Women receiving BCS with axillary dissection had lower 7-year breast cancer-specific mortality than did those without dissection (hazard ratio=0.53, 95% confidence interval: 0.44-0.63). We found a relationship between receipt of axillary dissection and radiotherapy on survival of older women after BCS. Women who received either axillary dissection or radiotherapy experienced similar survivals to those who received both axillary dissection and radiation, while women who received neither treatment experienced poorer survival (hazard ratio=1.76, 1.23-2.52), after controlling for demographics, tumor size and comorbidity. In conclusion, women who receive neither axillary dissection nor radiation therapy after BCS experience an increased risk of death from breast cancer. The lack of improvement in the past two decades in survival of older women with breast cancer may be explained in part by the increasing use of treatments that do not address potential tumor in axillary nodes.

Key words: breast cancer; axillary node dissection; breast-conserving surgery; survival.

Introduction

Axillary node dissection is a component of modified radical mastectomy, and also is commonly used in breast conserving surgery. There are two major rationales for axillary dissection (1-3). First, it physically removes potentially cancerous tissue in the axilla. Second, it allows for adequate staging information as a guide to more appropriate therapy. It could be argued that these two rationales are less compelling today than in the 1980's and before. For example, radiotherapy to the axillary nodes would accomplish a similar goal to physical removal of cancerous tissue (4). Also, increased use of adjuvant chemotherapy in early stage breast cancer means that the distinction between local and regional cancer may have less impact on choice of therapy now than it did before.

The reasons outlined above have led some authorities to question the wisdom of routine axillary dissection (5-8), and this is reflected in an increasing percentage of women with early stage breast cancer who do not receive axillary dissection as part of initial treatment (1, 9-11).

On the other hand, there are serious concerns raised by the omission of axillary dissection. It would appear that substantial numbers of older women who do not receive axillary dissection also are not receiving radiation therapy or chemotherapy (1, 10-13). Approximately 20-50% of women with early stage breast cancer will have positive axillary nodes found on axillary dissection (1, 14-16). In most women with axillary node metastases there is no indication of metastases on clinical palpation of the axilla (14-20). Even women with very small primary tumors of 0.5 to 1.0 cm in size have a greater than 10% incidence of axillary node metastases (1,

15-21). It would appear that many of these women are receiving no therapy directed against the axillary node tumor (1, 10-13, 15).

Therefore, we hypothesize that the failure to perform axillary dissection is associated with decreased survival in women diagnosed with early stage breast cancer. To test this hypothesis we examined the survival difference between older breast cancer patients receiving axillary dissection and those without axillary dissection, and examined the role of radiation therapy, chemotherapy and comorbidity. We used a data base in which information from the Surveillance, Epidemiology and End Results (SEER) registry was linked to Medicare Part A and B files (22-25). This allows us to better consider factors such as adjuvant radiation therapy and chemotherapy, as well as control for comorbidity, in survival analyses.

MATERIALS AND METHODS

Data Sources

We used two data sources: (1) the Surveillance, Epidemiology and End Results (SEER) 1973-96 Public Use Data Set, and (2) the merged SEER-Medicare database. The SEER program supports population-based tumor registries in four metropolitan areas (San Francisco/Oakland, Detroit, Atlanta, and Seattle) and five states (Connecticut, Iowa, New Mexico, Utah, and Hawaii), covering approximately 10% of the U.S. population (26). Since 1992 SEER registries included 11 areas, accounting for about 14% of the U.S. population (26). Information includes tumor location, size and histologic type; demographic characteristics such as age, gender, race and marital status; and types of treatment provided within four months after the date of diagnosis

(27). The SEER data set does not contain information on comorbidity, and information on chemotherapy and radiation therapy is considered incomplete (22, 23, 25, 28).

The Medicare claims data used in the study included inpatient hospital claims; claims for outpatient facility services, including ambulatory surgery; and claims for physicians' and other medical services. Cases reported by the SEER registries from 1991 to 1996 have been matched against the Medicare master enrollment file. The method of linking these data has been described elsewhere (22). This study was approved by the Institution's Review Board.

Study Population

Two study populations were analyzed separately. From the SEER Public Use Data Set, 26,290 female patients aged 25 and older women diagnosed with breast cancer between 1988 and 1993, who were diagnosed with early stage breast cancer, i.e. the American Joint Committee on Cancer (AJCC) stages I or II, and who received breast-conserving surgery, were selected for the analysis. Cases diagnosed before 1988 were not selected because information on tumor size was only available after 1988. Since the last date of follow-up was December 31, 1996, it allows the 3-year survival rate to be calculated in cases diagnosed in 1988-1993 and the 7-year survival rate for 6,318 cases diagnosed in 1988-89.

The SEER-Medicare linked database was used to examine the use of radiation therapy and chemotherapy and to determine comorbidity levels for cases diagnosed between 1991 and 1993. These years were studied because Medicare claims were available for all incident cases diagnosed beginning in 1991. In the SEER-Medicare linked data, after excluding those without

both Medicare Part A and Part B in the year of diagnosis, the study population were 14,089 women diagnosed with early stage (AJCC stage I or stage II) breast cancer at age 65 and older in 1991-1993. After excluding those who received mastectomy, or received no cancer directed surgery, or had missing information on the months of diagnosis, 5,328 who received breast-conserving surgery were included in the analysis.

Treatment and survival

Surgery and axillary dissection. In SEER, breast-conserving surgery (BCS) was defined as segmental mastectomy, lumpectomy, quadrantectomy, tylectomy, wedge resection, nipple resection, excisional biopsy, or partial mastectomy unspecified, with or without dissection of axillary lymph nodes (27).

Radiation therapy. We have previously shown that combining data from SEER and Medicare provided more complete information on radiation therapy (23). As previously described, receipt of radiation therapy was determined from SEER, supplemented by review of Medicare claims for radiation therapy within 4 months after diagnosis.

Chemotherapy. Chemotherapy was ascertained from the Medicare data through procedure and revenue center codes on at least one claim for chemotherapy made within 12 months after diagnosis of breast cancer. These codes included the ICD-9-CM procedure code of 9925 for a hospital inpatient or outpatient facility claim of chemotherapy (injection or infusion of cancer chemotherapeutic substance) (29), the Common Procedure Terminology codes of 96400-96549, J9000-J9999, and Q0083-Q0085 for a physician or outpatient claim of chemotherapy

administration (30, 31), and revenue center codes of 0331 (chemotherapy injected), 0332 (chemotherapy oral) and 0335 (chemotherapy intravenous) for an outpatient claim of chemotherapy (32). The ICD-9-CM V codes (29) of V58.1, V66.2, or V67.2 for follow-up examination or care after chemotherapy was also used, that generated 3 additional cases in the category of receiving chemotherapy within 12 months of diagnosis.

Comorbidity index. Comorbidity was ascertained from the Medicare data through ICD-9-CM diagnoses or procedures on claims made 2 years prior to the diagnosis of breast cancer. We used the comorbidity index created by Charlson (33) and later validated by Romano and colleagues using the ICD-9-CM diagnosis and procedure codes (34). Comorbidity scores were calculated for each patient. Both the Medicare inpatient and outpatient claims were searched for comorbid conditions, but not including breast cancer diagnosis codes (ICD-9-CM codes of 174x). Patients who had no inpatient or outpatient Medicare claims during this period were coded as a separate category.

Mortality and Survival Time. Breast cancer-specific death was defined similar to the method of the Early Breast Cancer Trialists' Collaborative Group (4): if patients died of breast cancer as an underlying cause of death, or if patients with breast cancer died of unknown causes. Information on months of survival from the date of diagnosis was provided in SEER. The last date of the follow-up for this cohort was December 31, 1996. This would allow analyses on the 7-year survival in women diagnosed with breast cancer in 1988-1989 from SEER Public Use Data, and 3-year survival among women diagnosed in 1991-1993 from the SEER-Medicare linked data.

Analysis

After patients who were lost to follow-up or died of other diseases were censored, a 7-year Kaplan-Meier survival curve was produced using the LIFETEST procedure for women diagnosed with breast cancer in 1988-1989 (35). In a separate analysis, all deaths in the first four years were censored and a survival curve from 4 to 7 years was constructed, in order to reduce any effect of comorbidity which might be expected to differentially affect early deaths. The log rank test was used to assess differences among the survival curves. In addition, the Cox proportional hazard model was used in the survival analyses using the PHREG procedure available in the SAS statistical package (35). These analyses took into account possible confounding factors such as age, race, marital status, cancer stage, tumor size, SEER area, and comorbidity level.

RESULTS

Table 1 presents the percentages of women receiving breast-conserving surgery (BCS) with or without axillary dissection by patient and tumor characteristics. Overall, 27% of all women with early stage breast cancer who underwent BCS did not receive axillary dissection as part of initial surgical treatment. Older women, unmarried women and those with very small (<0.5 cm) or very large tumors (≥ 4.0 cm) were less likely to receive axillary dissection. Overall, 74% of women who received BCS without axillary dissection were aged 65 or older. The data on the percentages receiving axillary dissection by stage are misleading, because the major means of distinguishing regional from local stage is by axillary dissection. Thus there is a

misclassification bias of underreporting regional stage tumor in women without axillary dissection. Because of this, in the survival analyses we control for tumor size rather than stage.

Figure 1 presents Kaplan-Meier survival curves of the 7-year breast cancer specific survival for women receiving BCS with or without axillary dissection. Survival was significantly greater for women with axillary dissection as compared to those without axillary dissection ($P < 0.0001$). The hazard ratio for mortality at seven years was 0.53 (0.44-0.63) for women with axillary dissection as compared with those without, after adjusting for age, marital status, race, tumor size and SEER area. There was also a significant difference in the survival curves between years 4 and 7 ($P < 0.0001$) after deaths in the first 3 years were censored as a crude control for comorbidity.

As discussed in the Introduction, axillary dissection may be less important if patients not receiving axillary dissection receive adjuvant radiation therapy or chemotherapy. We investigated this issue in women aged 65 and over diagnosed with early stage breast cancer between 1991 and 1993 using the SEER-Medicare linked data, which provides information on radiation therapy, chemotherapy, and comorbid conditions (22-25). Table 2 presents the percentage of women receiving radiation and chemotherapy as a function of receipt of axillary node dissection. Only 38% women who underwent BCS without axillary dissection received radiotherapy, compared to 86% of women who underwent BCS with axillary dissection. Very few of these older women received chemotherapy after BCS. Women who underwent BCS with axillary dissection were somewhat more likely to receive chemotherapy than women who underwent BCS without dissection (8.0% vs 3.1%). Use of radiotherapy did not vary greatly by

whether the axillary nodes were positive or negative or by estrogen receptor status, while use of chemotherapy was greater in women with axillary node metastases or with estrogen receptor negative tumors.

Table 3 presents the relationship between axillary dissection and receipt of radiation therapy on mortality of women aged 65 and older with early stage breast cancer. Women receiving neither axillary dissection nor radiotherapy were at a significantly higher risk for death, compared to those who received both axillary dissection and radiation therapy. Women receiving either radiation alone without axillary dissection, or axillary dissection without radiation were not at significantly higher risk for death, after adjusting for tumor size, estrogen receptor status, comorbidity scores, and other patient characteristics.

DISCUSSION

The findings of this study can be summarized as follows. First, substantial numbers of older women receiving breast-conserving surgery do not receive axillary dissection. Second, of those women not receiving axillary dissection, most also do not receive either adjuvant radiation therapy or chemotherapy. In other words, they receive no therapy directed at occult cancer in the axillary nodes. The percentage of older women who receive no therapy to their axillary nodes has been steadily increasing over the past decade (1, 22, 36, 37). Third, patients receiving breast-conserving surgery without axillary dissection experience significantly worse survivals than those who do, after controlling for other factors known to affect survival. Finally, there is an interaction between receipt of axillary dissection and radiation therapy on survival, such that women who receive either axillary dissection or radiation therapy experience similar survivals to

those who receive both axillary dissection and radiation, while women who receive neither treatment experience substantially poorer survivals.

In randomized controlled trials of women receiving breast-conserving surgery for early stage breast cancer, axillary dissection has no impact on survival, while the present study and another recent report⁹ found a strong effect of axillary dissection on survival in women treated in the community. We will discuss several possible reasons for this difference.

First, in the randomized trials showing no survival advantage associated with axillary node dissection, all other therapies (e.g., radiation, chemotherapy) were held constant. In actual community practice, a major theoretical benefit of axillary dissection would be that the results would influence choice of other treatments. At least one RCT has results that directly support that interpretation. Cabanes and colleagues (38) randomized 658 patients with breast cancers < 3 cm in diameter to receive lumpectomy alone or lumpectomy plus axillary dissection. All patients received radiotherapy to the breast and axilla, but choice of chemotherapy and tamoxifen was left to the discretion of the treating physicians. Not surprisingly, the group receiving axillary dissection had a much higher percentage of patients classified as regional stage; these patients in turn were more likely to receive adjuvant therapies; and they experienced substantially lower overall five year mortality (relative risk of death for the group not receiving axillary dissection = 2.4, $P < 0.01$).

Second, follow-up of patients would be expected to be better in a randomized controlled trial than in the community. Local or regional recurrence of disease would be picked up early,

and appropriate therapy initiated, thus minimizing the impact of axillary dissection on survival. In the community, surveillance after initial treatment for breast cancer is sporadic. For example, 22% of women who underwent breast-conserving surgery without adjuvant radiotherapy did not receive any mammography in the 2 years after initial treatment (39).

A third potential explanation for the discrepancy between randomized controlled trials and population-based observational studies on the impact of axillary dissection on survival is possible selection bias in the community; that is, women with underlying comorbidity might be less likely to receive axillary dissection and also be at higher risk for death. However, it is important to note that we were assessing only breast cancer-specific mortality, not total mortality. In addition, controlling for underlying comorbidity did not appreciably affect the increased breast cancer-specific mortality associated with axillary dissection. Finally, eliminating all deaths in the first four years after diagnosis, as an additional control for comorbidity, did not eliminate the impact of axillary dissection on breast cancer-specific survival.

We found no difference in survival among those who received axillary dissection plus radiation versus radiation therapy alone. This was unexpected, because those receiving axillary dissection would be more likely to be correctly staged and therefore more likely to receive chemotherapy and other treatments (Table 2 and reference 21). One reason for this may be that too few women received chemotherapy for there to be a noticeable effect on survival (Table 2).

We should point out the limitations of this study. First, there is no information on why women did not have an axillary dissection. Second, information on chemotherapy from Medicare has not been well validated externally, and its completeness is unknown. However, our study on patterns of chemotherapy use would suggest that Medicare claims data are relatively complete and accurate in identifying chemotherapy use (25). In addition, as we previously demonstrated, the fact that Medicare data demonstrates good validity in other aspects of breast cancer care (radiation therapy and type of surgery) provides indirect support for the validity of information for chemotherapy in Medicare (23, 24). The information on radiation therapy from the combined sources of SEER and Medicare would appear to be complete (23). Third, there was no information on the use of sentinel node biopsy in SEER, although this procedure may have potential to be a replacement for routine axillary dissection. However, it has still not been confirmed for routine use (40), and it was unlikely to have been widely used during the study period. Finally, we have no information on whether the patients were taking estrogen antagonists. Because estrogen antagonists have been shown to improve survival from breast cancer (41), it is possible that women who underwent BCS without either axillary dissection or irradiation were also less likely to be prescribed estrogen antagonists, which in turn was responsible for the worse survival of these women. In other words, lack of axillary dissection and radiation therapy associated with BCS may be a marker for other less than adequate care, such as estrogen antagonist administration.

In conclusion, a substantial number of older women with early stage breast cancer in the United States receive BCS without axillary dissection, and most of those women also do not receive adjuvant radiation. This combination of no axillary dissection plus no radiation after

BCS is associated with an increased risk of deaths from breast cancer. Breast cancer survival has improved steadily over the past 25 years, except for older women (42, 43). The lack of improvement in the past two decades in survival of older women may be explained in part by the increasing numbers of older women who receive treatments that do not address potential tumor in the axillary nodes (1, 9).

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Table 1. Receipt of axillary dissection by women with breast cancer who received breast conserving surgery (BCS) between 1988 and 1993 in 9 SEER areas, by patient and tumor characteristics

Patient and tumor characteristics	Number (%) of women receiving BCS* without axillary dissection	Number (%) of women receiving BCS* with axillary dissection	Total
Age (years)			
25-54	931 (10.2)	8173 (89.8)	9104
55-64	835 (15.2)	4674 (84.8)	5509
65-74	1604 (26.0)	4573 (74.0)	6177
75+	3421 (62.2)	2079 (37.8)	5500
Race			
White	6021 (26.0)	17145 (74.0)	23166
Black	463 (26.1)	1313 (73.9)	1776
Other	252 (20.9)	955 (79.1)	1207
Unknown	55 (39.0)	86 (61.0)	141
Marital status			
Married	2588 (17.4)	12276 (82.6)	14864
Unmarried	3866 (36.0)	6876 (64.0)	10742
Unknown	337 (49.3)	347 (50.7)	684
Cancer stage			
Stage I	5143 (28.7)	12750 (71.3)	17893
Stage IIA	1442 (22.4)	4998 (77.6)	6440
Stage IIB	190 (10.8)	1564 (89.2)	1754
Stage II,NOS †	16 (7.9)	187 (92.1)	203
Tumor size (cm)			
<0.5	472 (38.9)	743 (61.1)	1225
0.5-<1.0	1294 (25.0)	3883 (75.0)	5177
1.0-<2.0	2857 (23.9)	9089 (76.1)	11946
2.0-<3.0	1362 (25.2)	4053 (74.8)	5415
3.0-<4.0	466 (30.4)	1066 (69.6)	1532
4.0+	324 (40.4)	478 (59.6)	802
Unknown size	16 (7.9)	187 (92.1)	203
Total	6791 (25.8)	19499 (74.2)	26290

* BCS denotes breast-conserving surgery.

† NOS - not specified.

Table 2. Receipt of radiation therapy and chemotherapy in women aged 65 and older who underwent breast conserving surgery in 1991 through 1993, with or without axillary node dissection*

Surgical treatment categories	Number of patients	Percent of women receiving radiation therapy †	Percent of women receiving chemotherapy ‡
breast conserving surgery without axillary dissection	2215	38.5	3.1
ER § positive	1439	39.0	2.0
ER negative	197	44.2	6.1
ER unknown	579	35.4	1.9
Breast conserving surgery with axillary dissection	3113	85.9	8.0
Node positive, and ER § positive	368	85.3	13.6
Node positive, and ER negative	72	79.2	34.7
Node positive, and ER unknown	87	81.6	16.1
Node negative, and ER positive	1680	88.0	1.8
Node negative, and ER negative	306	86.6	9.8
Node negative, and ER unknown	534	83.5	2.1
Node not examined	66	62.1	4.6

* For women with early stage (local or regional) breast cancer diagnosed between 1991 and 1993 from the SEER-Medicare linked database.

† Radiation therapy was defined if SEER data indicated so or if there were Medicare claims for radiation therapy within 4 months after diagnosis of breast cancer.

‡ Chemotherapy was defined if patients had at least one Medicare claim for chemotherapy within 12 months after diagnosis.

§ ER denotes estrogen receptor status.

Table 3. Interaction between receipt of axillary dissection and radiation therapy on breast cancer survival in women aged 65 and older with early stage breast cancer, 1991-1993

Variables	Number of patients (n=5328)	Hazard ratio for 3-year breast cancer specific mortality (95% CI) †
Patients receiving BCS, by receipt of axillary dissection (Ax) and radiation (XRT)*		
No Ax + no XRT	1362	1.80 (1.26-2.58)
No Ax + XRT	853	1.13 (0.74-1.73)
Ax + no XRT	440	1.01 (0.59-1.71)
Ax + XRT	2673	1.00
Other key risk factors in the model		
Age (years)		
65-69	1287	1.00
70-74	1415	1.04 (0.69-1.56)
75-79	1189	1.04 (0.68-1.60)
80+	1437	1.21 (0.79-1.86)
Tumor size (cm)		
<0.5	264	1.00
0.5-<1.0	1252	1.17 (0.44-3.10)
1.0-<2.0	2419	2.21 (0.89-5.51)
2.0-<3.0	968	3.51 (1.39-8.86)
3.0-<4.0	255	6.99 (2.69-18.17)
4.0+	138	5.84 (2.11-16.19)
Unknown size	32	6.60 (1.54-28.28)
Comorbidity index scores ‡		
No Medicare claims	344	0.86 (0.46-1.60)
0	3616	1.00
1	637	1.55 (1.07-2.24)
2	323	1.77 (1.11-2.81)
3+	408	1.95 (1.30-2.91)

* BCS (breast-conserving surgery), No Ax (no axillary dissection); no XRT (no radiation therapy); Ax (axillary dissection); XRT (radiation therapy).

† Hazard ratios (95% confidence interval), adjusted for the variables listed in the table and also adjusted for marital status (married, unmarried and unknown), race (white, black, and other), 9 SEER areas, and estrogen receptor status (positive, negative, unknown).

‡ Comorbidity was assessed by a validated algorithm^{33,34} using Medicare claims.

Legend for Figure 1.

Figure 1. Kaplan-Meier breast cancer specific survival curve for women with early stage breast cancer, stratified by breast-conserving surgery (BCS) with and without axillary dissection.

The 7-year breast cancer specific survival curves are shown for women diagnosed with breast cancer diagnosed in 1988-1989. The log rank test for survival curves between BCS without axillary dissection and BCS with axillary dissection was statistically significant for two groups ($P < 0.0001$). Data are for all women aged 25 and older diagnosed with early stage breast cancer in one of the 9 SEER areas in 1988 and 1989 ($n=6,318$), and followed through 1996 from SEER Public Use Data Set.

